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ARCHIVES OF PATHOLOGY

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CHLOROFORM CONTENT OF THE BRAIN FOLLOWING ANESTHESIA*

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The problem of determining the chloroform content of the brain following anesthesia suggested itself to us as a direct result of a medicolegal case, involving our aid in the solution of the same.

A woman, aged 35 years, died in a doctor's office. An autopsy, performed by Dr. Charles Norris, Medical Examiner of the city of New York, disclosed perforation of the posterior vaginal vault, with the presence of about 300 cc. of blood in the peritoneum, but no evidence of peritonitis. Parts of the liver, brain and lungs were submitted to one of us (A. O. G.) for chemical analysis. Chloroform was found present. The amount in the lungs was 52 mg. in 1,000 Gm. The estimated amount of chloroform in 1,000 Gm. of brain was 156 mg. These results were compared with the values found in our series of cases in which death occurred during chloroform anesthesia or following the administration of chloroform with suicidal or homicidal intent (see table 1).

The figures in table 1 indicate that the brain of a person sufficiently anesthetized for a minor operation contains between 120 and 182 mg. of chloroform in 1,000 Gm. of brain tissue. In the case under discussion, the chloroform content of the brain was 156 mg. in 1,000 Gm. of tissue. This figure falls within the amount needed for complete mild anesthesia. An excessive amount of chloroform was not present. (An excessive amount ranges between 372 mg. and 480 mg.—cases 1 to 7.) The cause of death in the case under discussion was therefore given as hemorrhage following an incomplete abortion.

The doctor in whose office the woman was found maintained that he administered no chloroform; that he performed no operation of any kind; that the woman came to him to be treated and died before he could attend her. In order to prove or disprove the doctor's contention, the determination of the chloroform content of the brain and lungs

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was of vital importance. Chloroform was present in the organs of the woman. Where was it administered? In the doctor's office or somewhere else? If administered at some other place, how soon after coming out of the anesthesia did the woman feel well enough to walk? The cells continually ridding the organism of chloroform, how much chloroform could remain in her brain on her arrival at the doctor's office? These are the questions we were asked to answer.

On looking over the figures of table 1, we find that in the case of persons anesthetized for minor operations, the chloroform content is between 120 mg. and 182 mg. in 1,000 Gm. of brain. The case in question had 156 mg., indicating that the deceased person was under the influence of chloroform and therefore not able to walk; hence, the chloroform must have been administered on the premises.

TABLE 1.—*Chloroform Content of the Brain in Cases in Which Death Involved the Administration of Chloroform*

Case	History	Mg. Chloroform in 1,000 Gm. Brain
1	Suicide by inhalation	432
2	Suicide by inhalation	480
3	Suicide by inhalation	410
4	Suicide by inhalation	390
5	Homicide by inhalation	372
6	Homicide by inhalation	384
7	Homicide by inhalation	374
8	Anesthesia for abortion, shock	162
9*	Anesthesia for abortion, hemorrhage	60
10	Anesthesia for operation on tonsils, shock	136
11	Anesthesia for minor operation, shock	135
12	Anesthesia for minor operation, shock	145
13	Anesthesia for minor operation, shock	120
14	Anesthesia for minor operation, shock	122
15	Anesthesia for abortion, shock	182
16†	Anesthesia for minor operation, shock	70

* Patient came out of anesthesia; died of hemorrhage.
† Patient died from shock during administration of chloroform; was not fully anesthetized.

It seemed important to investigate this problem further by means of experiments on animals, to determine how soon after chloroform anesthesia the individual is again able to walk normally, and how much chloroform is present in the brain at varying intervals of time after the administration of chloroform. The present report is based on this work.

TECHNIC OF EXPERIMENTS ON ANIMALS

Ten dogs were used in these experiments. After being tied to the animal board, they were anesthetized with chloroform, the open mask method being used. They were kept in a state of surgical anesthesia for definite periods. The mask was then removed, and the animals were allowed to recover spontaneously. Dog 6 was not allowed to recover, but was killed by excessive administration of chloroform. In dogs 5 and 7, the trachea was clamped while they were fully anesthetized. In order to investigate the chloroform content of the brain at various stages of recov-

ery, the dogs were killed at stated intervals, as indicated in the chart. Painless death was obtained by injecting morphine and then exposing and clamping the trachea. Autopsy was then performed. The brain and lungs were removed, weighed and placed in the icebox in sealed containers until the analysis was started.

Method of Analysis.—The brain and lungs, when ice-cold, were ground up, and quickly placed in a 500 cc. distillation flask; about 100 cc. of water was added and also a little tartaric acid, enough to make the mixture acid in reaction. The material was then subjected to steam distillation, a long, well cooled condenser and an adapter being used. The receptacle for collecting the distillate, a 300 cc. Erlenmeyer flask, contained about 10 cc. of ice-cold, acidified (HCl) water and was packed in ice. The tip of the adapter reached into the ice-cold water contained in the receptacle for distillate. With these precautions, there was no loss of chloroform during distillation. Our experiments have proved that, if 250 cc. of distillate is collected, all of the chloroform in the tissues will have passed into the distillate. The distillate was well mixed, measured, stoppered and kept cold; 5 cc. portions of this distillate were taken for the colorimetric determination.

Colorimetric Estimation of Chloroform in Distillate.—The materials necessary for the colorimetric estimation of the chloroform in the distillate were: chemically pure pyridine (colorless), 20 per cent sodium hydroxide solution, and the standards to be described.

Chloroform Standards: One gram of pure chloroform was weighed out. This was done by placing a little more than 1 Gm. of chloroform into a weighing bottle with a ground glass stopper, allowing the chloroform to evaporate spontaneously and weighing from time to time (with weighing bottle stoppered) until the weight of the chloroform in the bottle was just 1 Gm. This gram of chloroform was then dissolved in about 900 cc. of water contained in a 1 liter volumetric flask; 5 cc. of hydrochloric acid was added, and finally enough water was added to bring the total volume to exactly 1 liter. The whole was thoroughly mixed. Precautions were taken to avoid evaporation of the chloroform during the transfer. This solution contained 1 mg. of chloroform in each cubic centimeter. From this stock solution, a series of weaker standards were made, having the following chloroform values: 0.5 mg. in 1 cc.; 0.1 mg. in 1 cc.; 0.01 mg. in 1 cc.; 0.005 mg. in 1 cc.; 0.0025 mg. in 1 cc. These standards do not keep; new standards were made for each set of determinations.

Procedure: Into five clean, dry, 50 cc. test tubes were pipetted 5 cc. portions of the five standards containing, respectively, 0.5 mg., 0.1 mg., 0.01 mg., 0.005 mg. and 0.0025 mg. of chloroform per cubic centimeter (see preparation of standards). Into a similar test tube was pipetted 5 cc. of the distillate. To each of the tubes, 5 cc. of chemically pure (colorless) pyridine and 10 cc. of 20 per cent sodium hydroxide solution were added. The contents of each tube were mixed and the tube loosely corked to avoid evaporation. The tubes were placed in a boiling water bath for exactly one minute and then quickly cooled by running water; 20 cc. of water was added to each tube, and the contents were mixed. Of the series of standards, the one that matched the color of the unknown closest was used as the standard and read against the unknown in the colorimeter.[1]

Calculation

$$\frac{\text{Standard}}{\text{Unknown}} \times \begin{matrix}\text{Value of standard used in} \\ \text{milligrams of chlorform}\end{matrix} \times \frac{250}{5} \times 1.087 \left\{\begin{matrix}\text{correction for per-} \\ \text{centage of recovery}\end{matrix}\right\}^{1} = \text{milligrams of chloroform in grams of tissue used}$$

1. Gettler, A. O., and Blume, Hyman: Chloroform in Brain, Lungs and Liver; Quantitative Recovery and Determination, Arch. Path. **11**:554, 1931.

RESULTS OF ANALYSES

The results, which are charted in table 2, indicate the following (all values calculated to 1,000 Gm. of brain tissue):

An animal killed by excessive administration of chloroform had 551 mg. of chloroform in the brain. Animals killed while in chloroform anesthesia had 270 mg. and 284.6 mg. of chloroform in the brain. Animals that were allowed to recover from the anesthesia showed a rapid decrease in the chloroform content of the brain, i. e.: after 34 minutes, 51.3 mg.; after 50 minutes, 33.3 mg.; after 65 minutes, 32.6 mg.; after 95 minutes, 23.6 mg.; after 102 minutes, 10.6 mg.; after 186 minutes, 5.2 mg., and after 190 minutes, 0.16 mg.

TABLE 2.—*The Rate of Disappearance of Chloroform from the Dog's Brain During Recovery from Anesthesia*

			Time in Minutes							Mg. of Chloroform in Brain at Death	
				Until First Signs of Recovery	At Which Until						
Dog	Body Weight, Kg.	Weight of Brain, Gm.	To Anesthetize		Until Placed on Floor	Hind Legs Were Still Ataxic	Dog Began to Look Normal	Until Death	Between Normal Appearance and Death	In Entire Brain	Calculated† to 1,000 Gm. of Brain
1	8.5	80	15	6	8	19	*	34	*	4.10	51.3
2	5.7	75	15	5	17	30	35	50	15	2.50	33.3
3	6.3	69	15	4	6	13	30	65	35	2.25	32.6
4	6.9	70	15	6	10	75	*	95	*	1.65	23.6
5	9.4	82	12	5	10	35	45	102	57	0.87	10.6
6	5.2	52	15	5	6	30	42	186	144	0.27	5.2
7	11.3	60	15	4	8	25	30	190	160	0.01	0.16
8	7.6	60	15	Trachea clamped while completely anesthetized						16.20	270.0
9	6.3	65	15	Trachea clamped while completely anesthetized						18.50	284.6
10	7.6	68	7	Killed by excessive administration of chloroform						37.50	551.5

* Morphine injected while animal was still ataxic.

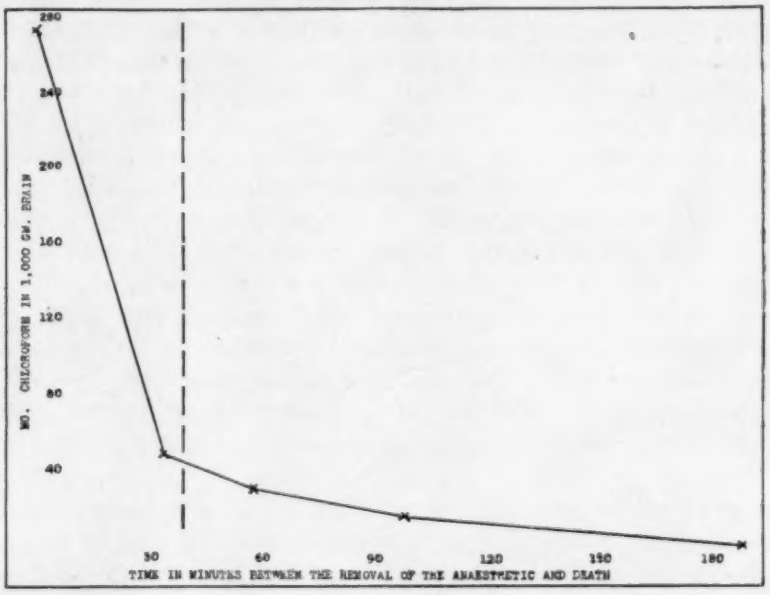
† Chloroform content of human brain is best reported on 1,000 Gm. basis; in order to facilitate comparison, the chloroform in the dogs' brains was also calculated to 1,000 Gm. portions.

It was between thirty and forty-five minutes before the dogs looked normal and could walk normally. Dog 1 probably was killed just as it was beginning to return to normal. It had 51.3 mg. of chloroform in the brain. Fifteen minutes after dog 2 seemed normal, it had 33.3 mg. of chloroform left in the brain, calculated to 1,000 Gm. of tissue. Thirty-five minutes after dog 3 seemed normal, it had only 32.6 mg. This is an indication that from fifteen to thirty minutes after the animal seems normal, the brain contains only from 30 to 35 mg. of chloroform in 1,000 Gm.

The lungs in some of the dogs were also analyzed. The values are not charted. We found that in the recovery stage the lungs contained only from 33 to 50 per cent of the amount of chloroform found in the brain.

The chloroform content of the brain of the deceased person in question was 156 mg. in 1,000 Gm. of tissue. On the basis of the determined figures, we hold that: The woman at the time of her death was still under chloroform anesthesia and not in a condition to walk. With 50 mg. of chloroform or thereabouts per thousand grams of brain tissue, she would have shown the first indication of normal coordination. If it took her only from fifteen to thirty minutes to get to the doctor's office, her brain should contain at the most from 30 to 35 mg. of chloroform.

The various points determined in our experimental work are vividly brought out by plotting milligrams of chloroform in 1,000 Gm. of brain



against time in minutes, as in the accompanying chart. Attention might be called to the following points brought out by the plotted curve: When animals which have been in full chloroform anesthesia are allowed to recover, the chloroform content of the brain drops rapidly. In our experiments, in 34 minutes it dropped from 278 mg. to 51.3 mg.; in 58 minutes it was down to 33 mg. From this point on, the chloroform kept decreasing, but more slowly. After 188 minutes, only 2.7 mg. of chloroform in 1,000 Gm. were left (average values for dogs 6 and 7). In the chart, the vertical dash line at the 40-minute interval indicates the point at which the animals first began to appear normal again. Eighteen minutes after the animals seemed normal, the brain contained only 33 mg. of chloroform in 1,000 Gm.

SUMMARY

A dog killed by the excessive administration of chloroform contained in the brain 551.5 mg. of chloroform in 1,000 Gm. of tissue. Animals while fully anesthetized with chloroform contained in the brain 270 mg. and 284.6 mg. in 1,000 Gm. of tissue. When an animal was in the stage of recovery, the chloroform content of the brain dropped very rapidly during the first 34 minutes, so that only 51.3 mg. in 1,000 Gm. of brain tissue was left. From then on, the chloroform content decreased more slowly, and after 190 minutes there was only 0.16 mg. of chloroform present in 1,000 Gm. of brain. Animals appeared normal again after 40 minutes. At this time they probably had about 45 mg. of chloroform in 1,000 Gm. of brain. Fifteen to thirty minutes after the animals seemed normal, the brain contained 35 to 30 mg. of chloroform in 1,000 Gm. In the stage of recovery, the lungs contained much less chloroform than the brain.

LEIOMYOSARCOMA OF THE PLEURA

REPORT OF A CASE *

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Reports of primary sarcoma of the pleura are not numerous. Robbins,[1] in 1908, described a large fluid-containing sac filling the left side of the thoracic cavity in a woman; it was lined by a thickened and nodular pleura, which on microscopic examination was seen to be composed of a vascular tissue containing many spindle-shaped and irregularly shaped cells. Peripherally these cells invaded the subpleural adipose tissue. Metastases were present in the right lung and in the liver. From the literature Robbins summarized reports of ten instances of primary pleural sarcoma in which he believed the diagnosis reasonably certain. In 1908, Mehrdorf [2] reported a myxomatous fibrosarcoma in a 43 year old woman. The firm, well encapsulated tumor weighed 3,270 Gm. and filled the right side of the thoracic cavity. Microscopically there were many spindle-shaped cells in a connective tissue network, and myxomatous changes were found. There were no metastases. Pallasse and Roubier,[3] in 1915, described an enormous malignant lipoma of the pleura in a 75 year old woman, and in a 51 year old woman a fibrosarcoma weighing 2,500 Gm. They classified tumors of the pleura as benign, mixed and malignant, and grouped the latter into diffuse and circumscribed types.

More recently, Nevinny [4] found in the right side of the thoracic cavity of a 43 year old woman a tumor 18 cm. in diameter. It contained large, blood-filled spaces, and was enclosed in a well defined capsule. Microscopically, most of the cells were seen to be spindle-shaped. No metastases were present. Nevinny considered the tumor a primary giant cell sarcoma of the pleura. MacMahon and Mallory,[5] in 1928, described in detail a slowly progressing fibrosarcoma of the right side in a 71 year old white man. The thickened and nodular pleura lined a large

* Submitted for publication, Nov. 26, 1930.

* From the Department of Pathology of the Cook County Hospital.

1. Robbins, W. B.: Boston M. & S. J. **158**:691, 1908.
2. Mehrdorf, Robert: Virchows Arch. f. path. Anat. **193**:92, 1908.
3. Pallasse, E., and Roubier, C.: Ann. de méd. **3**:243, 1915.
4. Nevinny, Hans: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **40**:277, 1927.
5. MacMahon, H. E., and Mallory, G. K.: Am. J. Path. **4**:387, 1928.

sac containing 2,200 cc. of bloody fluid. Microscopically, cells varying from spindle shape to round and polymorphous, with single or multiple nuclei and many mitotic figures, were embedded in a collagenous connective tissue stroma.

In the cases of primary pleural sarcoma which have been mentioned and in those cited from the literature by these authors and by Grabow,[6] most of the tumors were grossly of either of two types. In one of these, the pleura was nodular and thick and enclosed a large sac filled with bloody fluid; in the other, there was a single, firm, usually enormous tissue mass. The two types were of approximately equal occurrence. The microscopic structure was not uniform, and most of the tumors were classified according to cell morphology.

The present report describes a histologically malignant primary tumor apparently originating from the smooth muscle of the pleura, which has been shown by Baltisberger[7] to be present in superficial and deep layers of definite bundles, as well as in the walls of blood vessels.

REPORT OF CASE

Clinical History.—On May 13, 1930, an 83 year old white widow, Austrian, without occupation, was admitted to Cook County Hospital. In the examining room a diagnosis of arteriosclerosis was made, and the patient was placed in the medical service of Dr. McMullen. Although apparently not acutely ill, she was confused, and no history was obtainable, aside from the statement that she had suffered from pain in the left side of the chest for two months.

Physical examination revealed a greatly emaciated, extremely restless, elderly woman. The temperature was 99.6 F.; the pulse rate, 76; the respiratory rate, 22, and the blood pressure 210 systolic and 100 diastolic. The thorax was long and narrow. The expansion of the chest was somewhat diminished on both sides. Many harsh rhonchi were heard over both lungs. The position and borders of the heart seemed normal, and a loud systolic murmur was best heard at the base. The liver was palpable 2 cm. below the costal margin, and the abdomen was distended, especially in the lower half. The arteries of the extremities were tortuous and hardened. No signs of intrathoracic tumor were elicited, and the patient's condition was diagnosed as hypertensive heart disease with generalized arteriosclerosis.

The patient continued to be restless and confused, and was occasionally violent. Her temperature varied between 97 and 98 F. until a terminal rise to 102.6 on June 8. She died on June 9, twenty-seven days after her entrance into the hospital and about three months after the onset of her illness.

Autopsy.—Seven hours after death autopsy was performed by Dr. R. H. Jaffé. The body was 154 cm. long and weighed 76 pounds (34.5 Kg.), with the abdomen four fingerbreadths below the level of the chest, and midline fat practically absent. The liver weighed 950 Gm., was adherent to the diaphragm, and extended 10 cm. below the xiphoid process and 3.5 cm. below the costal arch. The diaphragm was at the level of the sixth rib.

6. Grabow: Berl. klin. Wchnschr. **47**:1625, 1665 and 1707, 1910.
7. Baltisberger, Wilhelm: Ztschr. f. Anat. u. Entwicklung **61**:249, 1921.

The left side of the thoracic cavity was partly obliterated by fibrous adhesions. The upper lobe of the left lung was crepitant in its superior two-thirds and at the inferior tip, and the apex was much distended. The remaining part of this lobe and the entire lower lobe were airless and markedly compressed by a large, firm tumor mass, to which the lung was adherent in an area, 10 by 3 cm., over the lower lobe and by small fibrous tags near the hilus. The rounded tumor measured 22 cm. vertically, 18 cm. in transverse diameter, and 8 cm. antero-posteriorly. Its surface was firm, and smooth, except for a few slightly projecting nodules. Some of these at and near the superior pole of the mass, the largest 15 mm. in diameter, were a homogeneous deep red; others near the hilus of the lung, the largest 3 mm. in diameter, were pearly white. There was a moderate

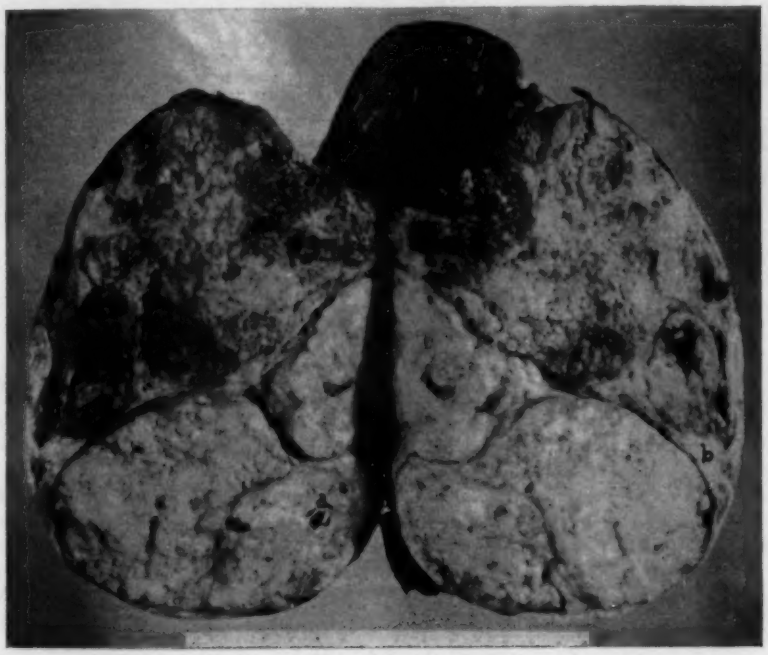

Fig. 1.—Leiomyosarcoma of the pleura (picture taken from the Kaiserling specimen): *a*, soft yellowish-gray tissue with openings into a cavity; *b*, light yellow nodule.

number of dilated small blood vessels, with occasional deep red spots ranging in size from that of a pinpoint to that of a pinhead. Elsewhere the surface was grayish white. The tumor was covered by thickened pleura, which bore numerous fibrous tags. On the cut surfaces (fig. 1) the tumor was seen to be composed of three roughly spherical nodes, the largest of which measured 15 by 9 by 7 cm., separated by smaller nodules. The surfaces of two of these nodes were firm, light gray and homogeneous, with numerous rounded orifices 1 mm. or less in diameter. In an area, 5 by 2 cm., in the lowermost node (fig. 1 *a*), the surfaces were softer and yellowish gray, with openings up to 6 mm. wide which led into an irregularly shaped cavity crossed by trabeculae of yellowish gray tissue. The superior, largest node was softer than the others, and was composed of a network

of interwoven gray and reddish-brown tissue. A nodule, 3 cm. by 1 cm., was soft and light yellow (fig. 1 *b*).

The visceral pleura over the left lung was smooth, except for a few small fibrous tags and the adhesions to the surface of the tumor. The bronchial mucosa was injected and thickened, the cartilaginous rings were calcified, and the bronchi were diffusely dilated and contained mucoid pus. The intima of the pulmonary arteries was smooth. The hilus and the mediastinal lymph nodes were soft, small and black. The right lung was distended, and in the right lower lobe was a fibrocaseous nodule 6 mm. in diameter. There were no tumor metastases in the lungs or elsewhere.

The other conditions found at autopsy were as follows: severe sclerosis of the coronary arteries, moderate atheroma of the aorta and of the peripheral arteries, dilatation of the heart and degeneration of the myocardium, arteriolosclerosis of the kidneys, brown atrophy of the liver, atrophy of the spleen, cholelithiasis, nodose goiter, atresia of the external uterine os and marked cachexia.

Microscopic Examination.—Tissue from the three nodes and from the light yellow nodule was taken for microscopic examination. The specimen had been fixed in Kaiserling's solution. Frozen sections were stained with sudan III and hematoxylin, hematoxylin and eosin, and with the Bielschowsky-Maresch silver impregnation. Paraffin sections were stained with hemalum and eosin, van Gieson's stain, Heidenhain's iron hematoxylin, Mallory's phosphotungstic acid and hematoxylin, Mallory's aniline blue, and Weigert's elastic stain.

The tumor of the left pleura consisted of interwoven bundles of tissues of two types. In one type the cell contained a large ovoid nucleus with delicate chromatin network. The cytoplasm, yellow with van Gieson's stain and red with Mallory's connective tissue stain, consisted of homogeneous, narrow bands prolonged from the nuclear poies or of delicate projections from the nuclear periphery. The other tissue was a fibrillar connective tissue, with deeply staining collagen bands, between which were long, flattened, darkly staining nuclei. Some parts of the tumor consisted almost wholly of cells of the first type, in a delicate connective tissue stroma. Such was the structure immediately adjacent to the pleura, about the blood vessels, and in irregularly distributed foci throughout the growth. In other regions the proportions of the two types were almost equal. Finally, there were parts in which the connective tissue was dominant, with only sparsely scattered cells of the first type. Such an arrangement was present immediately peripheral to necrotic parts of the tumor.

The mass was well encapsulated by the pleura, which was from 1 to 3 mm. thick. In this capsule, near the hilus of the left lung, the pleura contained distinct bundles of smooth muscle fibers that apparently passed rather abruptly into the large cells of the tumor. Between the visceral pleura of the left lung and the capsule of the tumor were a few strands of fibrillar connective tissue. The thickest parts of the capsule were composed of dense hyaline tissue.

Throughout the mass were numerous thin-walled small blood vessels. The elastic stain revealed only a very few fine, deep blue fibers in the walls of these vessels. Peripheral to some, the cells of the tumor were flattened and formed concentric whorls. Some of the vessels contained mixed thrombi; adjacent to these there were extravasation of blood, a moderate diffuse infiltration by lymphocytes, polymorphonuclear leukocytes and plasma cells and pyknosis of the nuclei of the tumor cells.

In disseminated regions there was complete necrosis, as in the small yellow area on the cut surface seen grossly. Numerous small foci of retrogressive changes were present, alternating in some parts with well stained areas that were

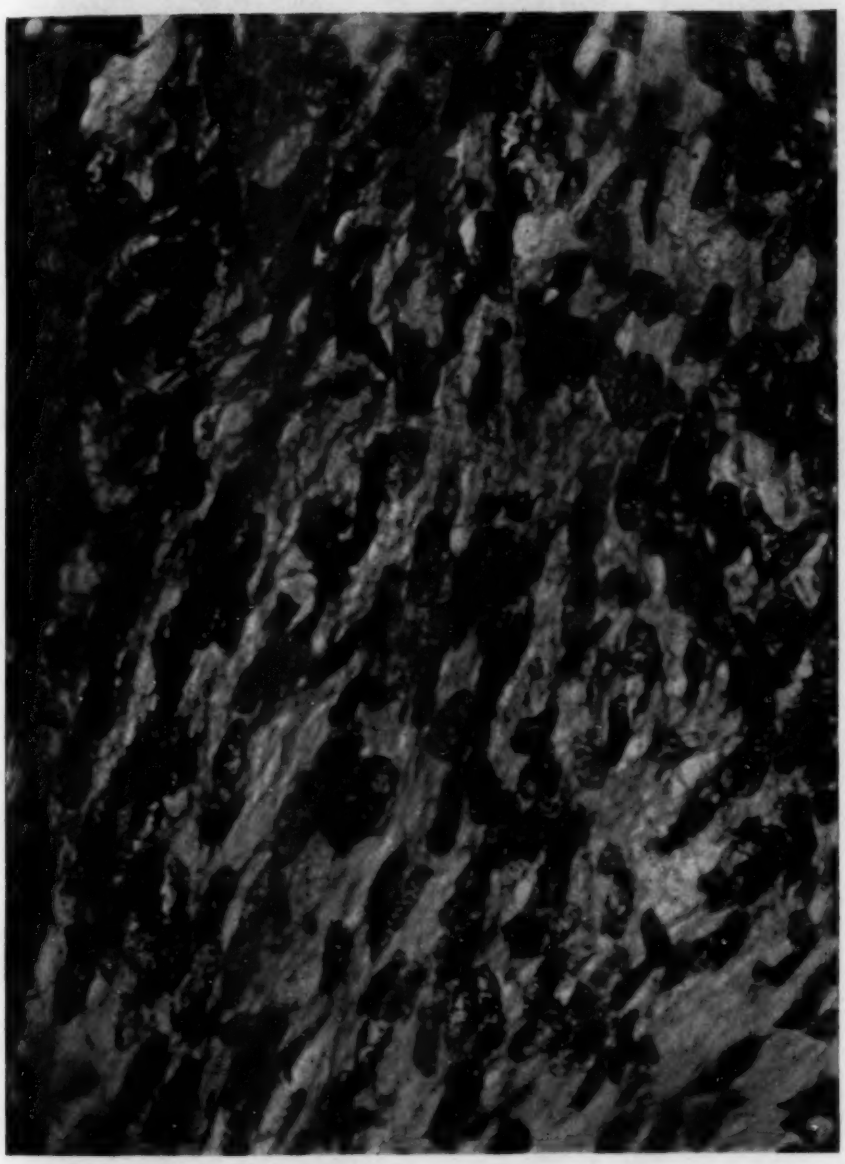

Fig. 2.—Area of great cellularity. Note the variation in size and shape of the nuclei of the blastomatous muscle fibers. Hemalum-eosin; × 800.

adjacent to blood vessels, and thus producing a peculiar patchy appearance. Where these retrogressive changes had occurred, in some places the nuclei were pale, the chromatin was indistinct, and there were fine fat droplets between the cells; in other parts there were polymorphonuclear leukocytes and lymphocytes, and finally, in regions nearly necrotic, the connective tissue was hyaline, and few nuclei were visible.

The left lung was not infiltrated by the tumor, but the alveoli near the periphery were markedly compressed, with some atelectasis. In the perivascular and peribronchial lymphatics were focal accumulations of polymorphonuclear leukocytes, and a few of the alveoli were filled by these cells. The bronchial epithelium was desquamated; the nuclei were pyknotic, and the cytoplasm was granular. The mucosa was densely infiltrated by lymphocytes. These cells were also grouped in perivascular and interstitial accumulations. The cartilage of the bronchi was calcified. The walls of the arteries and of the veins were thickened, and the capillaries were dilated. Mononuclear phagocytes contained small granules of dark brown pigment. There was moderate pigmentation of the lung with coal dust, and a few of the alveolar septums were clubbed.

The histology of the tumor was as follows: Nuclei were centrally placed in the large tumor cells (fig. 2). Most of these nuclei were ovoid or fusiform, but many appeared rounded or irregularly shaped, and some were slightly constricted in the central portion. In many of the cellular regions mentioned they were very large; in other parts they were smaller and narrower. All contained a fine chromatin net with coarse dots at the points of the crossing of the threads. There were no nucleoli. In most parts of the tumor a distinct nuclear membrane was present. There were very few mitotic figures. The cytoplasm was in most parts fusiform, extending from the two nuclear poles as homogeneous bands, but in some places it formed fine processes extending in various directions from the nucleus. Some of the cell tips were branched. No fibrils were visible in these cells, and the Bielschowsky silver impregnation revealed no intervening reticulum. The stroma was typical collagenous connective tissue. In some regions collagen formed closely adjacent broad bands; in other parts there were only fine fibrils about the large tumor cells. The connective tissue nuclei were larger and in some places more numerous than is usual.

COMMENT

Clinical examinations during the month that the patient was hospitalized did not lead to a diagnosis of intrathoracic tumor. The signs often associated with such a growth, such as dyspnea, visible protrusion of the wall of the chest and enlargement of the superficial veins, were not apparent. The clinical diagnosis of arteriosclerosis was confirmed at autopsy, at which the cause of death was found to be severe sclerosis of the coronary arteries. The pleural tumor was therefore incidental.

Primary pleural sarcomas of all sorts are rare, and I know of no report of a primary malignant smooth muscle tumor. In the present instance there were connective tissue fibers and nuclei throughout the mass, so that the term fibroleiomyosarcoma might be thought appropriate. Cells of other than connective tissue type were so dominant, however, and the signs of malignant changes in the nuclei of the connective tissue cells were so scarce, that the term leiomyosarcoma seems preferable.

Little can be said concerning the immediate cause of this tumor. The absence of an adequate clinical history makes it doubtful that pleuritis preceded the tumor. Such a process was observed clinically in the patients whose pleural tumors were reported by Nevinny and by Kidd and Habershon.[8] The relation of such an inflammatory lesion to the formation of tumor is obscure.

The presence of a well defined capsule, the absence of metastases and the scarcity of mitotic figures, as well as the clinically benign nature of the tumor here described, may seem to demand a diagnosis of leiomyoma. But the heterotypic morphology of the growth, the decided variation in the size and shape of the nuclei of the tumor cells, and the marked anaplasia of these nuclei in many cellular regions speak for a histologically malignant tumor. It is well known that many malignant growths that attain a large size locally produce no metastases. The absence of metastatic foci in the bodies of persons with huge pleural sarcomas is pointed out by Nevinny in his own case and in the five from the literature that he considered of similar nature.

SUMMARY

A massive leiomyosarcoma of the pleura of the left side of the chest of an 83 year old white woman is reported and discussed.

The literature of primary pleural sarcomas is briefly reviewed. No report of a malignant smooth muscle tumor has been found.

8. Kidd, P. K., and Habershon, S. H.: Tr. Path. Soc. London **49**:15, 1898.

FLEXNER-JOBLING RAT CARCINOMA

EFFECT OF FEEDING LIVER AND MUSCLE ON GROWTH OF TUMOR *

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AND

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The marked beneficial effect of the administration of liver to patients with pernicious anemia has stimulated the administration of this substance to patients with other pathologic conditions, including malignant diseases.[1] However, before these reports on the effect of the administration of liver to patients who had carcinoma were made, we had started the first of our series of experiments to ascertain the effect of liver on the growth of the Flexner-Jobling rat carcinoma. The results of these experiments were very definite and were reported.[2] However, the experiments did not disclose whether the effect observed was due to the liver specifically or to the diet high in protein. Accordingly, other experiments subsequently were performed in which the effect of the feeding of muscle also was observed.

There is some evidence that the liver might have a more or less specific relationship to the development of malignant conditions. An enormous amount of work has been done in an attempt to discover a relationship between lipoid metabolism and malignancy. Sufficient positive data have been secured to make the quest for this relationship interesting. The liver is a most outstanding organ concerning which an important function in regard to lipoid metabolism can be postulated. The hypothesis has been advanced from the embryonic point of view, based on the fact that the liver is relatively large in the fetus, that the liver might be of significance in malignant conditions. Therefore, as has been said, in accordance with this consideration,[3] liver has been administered to patients with carcinoma.

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* Submitted for publication, Dec. 9, 1930.

* From the Division of Experimental Surgery and Pathology, the Mayo Foundation.

1. Middleton, W. S.: The Erythropoietic Response of the Various Anemias to Liver Therapy, J. A. M. A. **91**:857, 1928. Strisower, R.: Die appetiterregende Wirkung der Liberdiät bei Krebs, Wien. med. Wchnschr. **77**:1754, 1927. Tuchfeld, H.: Pierre Marie'scher Osterarthropathie hypertrophiante pneumique, Wien. med. Wchnschr. **77**:815, 1927.

2. Caylor, H. D.: The Influence of Liver Feeding on the Rate of Growth of Flexner-Jobling Rat Carcinoma, Proc. Staff Meet., Mayo Clin. **3**:454, 1928.

3. Howitt, J. R.: Liver Extracts in Treatment of Malignant Disease, Nature **118**:263, 1926.

PROCEDURE

The Flexner-Jobling [4] rat carcinoma was the tumor used in all experiments. The recipients were white rats of known age. The animals were inoculated, by means of the trochar method,[5] with bits of living tumor tissue. Small groups of rats of the same age and size were inoculated at one time. Following the successful transplantation of the tumors the rats were divided into three groups, one group to be fed liver, one group a ration high in protein (fresh muscle) and one group the common maintenance ration, as a control. All of the animals were kept in the same room in cages of the same type. They were all fed one of two maintenance rations: either the ration suggested by Steenbock,[6] or a diet composed of bread and milk twice weekly, combined with oats and an occasional feeding of dog biscuit. Fresh liver was placed each day in the cage of the animals that were to be fed liver in addition to the regular ration, and fresh, uncooked muscle, in addition to the regular ration, was given to the group that was to be fed a ration high in protein. The liver and muscle were usually consumed.

The ages of the animals at the time of inoculation with the tumor varied from 23 to 120 days. Under ether anesthesia, transplantation was made into the subcutaneous tissue of the back of each animal. Measurements of the two transverse dimensions of the tumor were made with calipers when the tumor was sufficiently large (usually about 0.5 cm.) to permit correct measurement. These data were recorded, with the weight of the animal, changes in the general condition of the animal and changes in the tumor. The two dimensions of a tumor, namely, a and b (these measurements were usually at right angles to each other), being known, the volume of the tumor was assumed to be given approximately in arbitrary units by the formula $a \times b\ (a + b)$. Twenty-six control rats, twenty-nine rats that were fed liver and fifteen rats that were fed muscle were observed.

RESULTS

Early in the experiments it became evident that there were differences in the three groups of animals. These differences were evident in regard to the length of life after inoculation with the tumor and in regard to the volume of the tumor at the time of death.

The arithmetical averages of the numbers of days between inoculation of the animals with the neoplasm and the deaths of the animals were as follows: in the control group, 113 days; in the group that was fed liver, 90 days, and in the group that was fed a ration high in protein, 88 days. When these data were plotted on logarithmic probability paper, it was found that the curves for the group of animals that were fed liver and the group fed a diet high in protein were below the curve for the control group.

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4. Flexner, Simon; and Jobling, J. W.: Studies upon a Transplantable Rat Tumor Originally Regarded as a Sarcoma; Probably a Teratoma from Which an Adeno-Carcinoma Developed, Monographs, New York, Rockefeller Institute for Medical Research, 1910-1912, vol. 1-4, pp. 1-50.

5. Mann, F. C.: Attempts to Obtain Transplantable Tumor in the Higher Species of Animals, J. Cancer Research **4**:331, 1919.

6. Steenbock, H.: A Satisfactory Ration for Stock Rats, Science **58**:449, 1923.

The volume of the tumor at the time of death was almost always larger in the group of animals fed liver than in the control group. The ratio of the average volume of the tumor in the first group (fed liver) to the average volume of the tumor in the control group was 1.35 : 1. The results, plotted on logarithmic probability paper, revealed that the curves for the volume of the tumor in the control animals and in the animals fed on a ration high in protein, at the time of death, were almost always below the curve for the volume of the tumor in the animals fed liver.

It is noteworthy that after ulceration of the tumor there was usually diminution in the size of the lesion. This was probably due to the reduction of the internal pressure in the tumor, with the loss of substance of the carcinoma. In our experience with the Flexner-Jobling carcinoma, usually, when the lesion reached a size of from 1.5 to 2 cm., there was necrosis in the center of the tumor, and as the growth increased, the region of degeneration in the center increased, so that after about sixty days the neoplasm was composed of a thin rim of living, growing tumor tissue, whereas the bulk of the tumor was composed of carcinoma cells in various stages of degeneration.

It was furthermore worthy of note that in the group of rats fed liver there was no regression of the tumor in any rat, in contrast with the fact that in five of the fifteen rats fed fresh muscle and in seven of the twenty-six rats fed the control ration the tumors regressed.

SUMMARY AND CONCLUSION

From these data it is apparent that, following the transplantation of Flexner-Jobling rat carcinoma, the animals fed fresh liver or muscle as an adjunct to their regular ration lived for fewer days than did the animals fed the usual laboratory ration. At the time of death the volume of the tumor was larger in the animals fed liver than in the control group and the group given the ration high in protein. The number of days between the inoculation of the rat with the tumor and the ulceration of the growth was greater for the control group than for the rats fed liver. What element was supplied to the diet of the animals by the liver that apparently stimulated the growth of the tumor is not known, although the demonstrated stimulative effect of cholesterol and lecithin would suggest that these substances might have been responsible. It seems likely that the addition of liver or of a ration high in protein to the regular ration of the rats that were inoculated with the tumor increased the nutriment for the growth of the tumor, which probably should be considered much as a parasite. Although these observations were made in animals and with a transplanted tumor that cannot be considered the same as a spontaneous neoplasm growing in man, it would seem worth while to proceed very cautiously in the administration of liver to patients with carcinoma.

DISSEMINATED VENOFIBROSIS (PHLEBOSCLEROSIS)

ITS CLINICOPATHOLOGIC SIGNIFICANCE *

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Venous lesions, particularly venofibrosis, have, we believe, a far greater claim, than do hemorrhagic diatheses, to the facetious title of "step-child of pathology," bestowed on the latter by E. Frank.

Venofibrosis (phlebosclerosis) is not mentioned in Delafield and Prudden's "Textbook of Pathology" or in that of MacCallum. Beattie and Dickson mention merely that phlebo(veno)sclerosis is similar to thrombophlebitis and is said to occur in syphilis and gout. The classic German textbooks on pathology, Kaufmann's and Aschoff's, devote but a few lines to the subject. In the monumental pathologic encyclopedia edited by Henke and Lubarsch four pages are given to discussion of phlebosclerosis.

When one turns to the clinical significance of this condition, the information to be gleaned from the standard textbooks on clinical medicine is even more meager than that found in books on pathology: thus Barker's "Monographic Medicine" dismisses the subject with a few lines. This applies to textbooks, as well as to monographs. Only in the "Traité de médecine et de thérapeutique," by Gilbert and Thoinot, is considerable space devoted to the description of the lesions of the veins and to the discussion of phlebosclerosis—by Widal and Bezançon —in the most complete article on the subject.

INCIDENCE OF THE CONDITION

Judging by the paucity of the information contained in books, as well as in the current literature, one would naturally regard the condition as a clinical curiosity; we do not think it is. A series of 24 cases occurring within eight months in a small service of a 175 bed hospital after Dr. Hauswirth had called attention to disseminated venofibrosis in a young man, aged 31, and diagnosed his terminal condition as portal thrombovenosclerosis has convinced us that the condition cannot be rare. A search of the literature has corroborated our impression as to the relatively infrequent recognition of the condition.

* Submitted for publication, Nov. 8, 1930.

There are two interesting publications: one by Martin and Meakins [1] and the other by Martin and Tull.[2] Martin and Meakins "emphasize the fact that phlebosclerosis is of far greater frequency than is generally supposed, and more especially in young adults, without associated arteriosclerosis." They reported 31 cases, the ages of the patients ranging between 18 and 45, but especially between 20 and 30. In their opinion phlebosclerosis existed in 60 per cent of all patients examined by them. The pathologic and clinical data will be described further on. Martin and Tull found this condition in 12 of 30 children from 4 to 15 years of age. This opinion as to the relative frequency of the condition is shared by Widal and Bezançon [3] and Souques and Janvier.[4] Several cases were seen by Dr. Hauswirth in clinics other than our own.

PATHOLOGIC DATA

The lesion that we have been studying for the past few months has been referred to in the literature—when at all mentioned—under several names: hypertrophy of the veins, endophlebitis, hyperplastic phlebitis and phlebosclerosis. Neither phlebitis nor hyperplastic phlebitis seems to us a happy choice for the name of the lesion, since there does not appear to be any evidence of an inflammatory reaction in any of the veins that we have studied so far; the word "hypertrophy" would be a much better term were it not for the fact that, clinically, it conveys little information; we liked the term "venosclerosis" because the veins so affected feel exactly like sclerosed blood vessels, but had to abandon it because it gives the idea of a condition similar to arteriosclerosis-atheromatosis with calcification. We have decided to adopt the word "venofibrosis," notwithstanding that it carries with it the suggestion of there having been at one time an inflammatory process, although we have no morphologic evidence of it. Believing, as we do, that the process is primarily replacement fibrosis of the muscle of the media, as well as subendothelial fibrosis of the intima, we feel that the word "venofibrosis" is preferable.

Of the earlier investigators, Lobstein, who introduced the term "phlebosclerosis," thought it parallel in its histomechanics to arteriosclerosis. Sack [5] believed phlebo(veno)fibrosis, like arteriosclerosis, to be due to nutritional disturbance, with primary weakening of the media; according to him, the latter is followed by the dilatation of the

1. Martin, C. F., and Meakins, J. C.: Am. Med. **10**:611, 1905.
2. Martin, C. F., and Tull, J.: Arch. Pediat. **25**:191, 1908.
3. Widal and Bezançon, in Gilbert and Thoinot: Traité de médecine et de thérapeutique, Paris, Masson & Cie, 1927, vol. 1, p. 689.
4. Souques and Janvier, quoted by Widal and Bezançon (footnote 3).
5. Sack, E.: Virchows Arch. f. path. Anat. **112**:403, 1888.

lumen (phlebectasia) and, finally, by the proliferation of connective tissue, resulting in thickening of the intima. Sack believed that phlebo(veno)fibrosis occurs most frequently in the lower extremities, owing to greater changes in the hydrostatic pressure; our experience agrees with this observation.

Fischer [6] claimed that phlebo(veno)fibrosis is analogous to arteriosclerosis, and, like Koester and his pupils, he regarded it as an inflammatory process; he claimed to have found regularly some inflammatory changes in the walls of the veins, but admitted that there was no proliferation of elastic fibers (seemingly an argument against the similarity of phlebofibrosis and arteriosclerosis). Fischer pictured the inflammatory process as spreading from the vasa vasorum toward the intima, the elastic tissue resisting the inflammation the longest; the intima is protected by the internal elastic lamina, and when it is finally attacked, its involvement is focal—phlebofibrosis circumscripta. Fischer believed that the process occurs most frequently after the age of 35, and that the etiologic factors are largely those responsible for arteriosclerosis —"alcohol, gout, and syphilis."

Mehnert, quoted by Barach,[7] regarded veno(phlebo)fibrosis as either primary or secondary; the former shows weakening of the wall of the vessel and connective tissue proliferation of the intima, while the latter is due to a diffuse venous stasis.

Keya, also quoted by Barach, believed venofibrosis to be due to an abnormally increased functional demands on the veins by muscular effort, the thickened intima being a partial manifestation of the hypertrophic process; unlike Jores, however, he regarded the splitting of the elastic lamellae as a passive process.

Simmonds [8] did not regard phlebo (veno) fibrosis as an inflammatory process and assigned the etiologic rôle to lead, gout and syphilis; according to him, the lesion comprises degenerative changes in the intima and hypertrophy with degenerative changes of the media. Simmonds stressed the fact that none of his seven cases showed any inflammatory picture, although they were observed in different stages of the disease; none of his sections showed any cellular infiltration, scar tissue or periphlebitic changes (this, of course, militates, according to Benda, very strongly against the syphilitic nature of the lesion).

The opinions at our disposal are obviously far from unanimous. On the one hand, we have the opinion of Simmonds, Sack, Weitzmann, Mehnert, Neumann, Manchat, Zwingmann, Dmitrijeff and others, that venofibrosis is not an inflammatory lesion; on the other hand, the opinion

6. Fischer, B.: Beitr. z. path. Anat. u. z. allg. Path. **27**:494, 1900.
7. Barach: Beitr. z. path. Anat. u. z. allg. Path. **50**:71, 1911.
8. Simmonds: Virchows Arch. f. path. Anat. **207**:360, 1912.

of Fischer, Koester and his pupils, who believed that it is. Some of the adherents of the theory that the lesion is noninflammatory regard venofibrosis as a reparative process, while Sack and his school expressed the belief that it is a nutritional disturbance. Other authors regard the process as similar to arteriosclerosis, while some deny this. As to the etiologic factors, some favor infection (syphilis); others see the true cause in chemical poisons (e. g., lead), while still others look on it as a result of a metabolic disorder (e. g., gout).

Of the recent writers on the subject, Benda[9] seemed inclined to regard phlebo(veno)fibrosis as a senile atrophic process and one not parallel to arteriosclerosis.

Our own observations on over thirty veins can be summarized as follows: Vessels are always small, never dilated. We have never seen any inflammatory changes, such as cellular infiltration, scar formation, edema, necrosis, etc.; frozen sections have never shown fatty droplets, nor have we ever seen calcium deposits. The histologic changes seem to be uniform and constant. The very earliest changes seem to be the loss of the endothelium and the hyalinization of the denuded surface. There is a marked hyperplasia of fibrous connective tissue, particularly in the media, and to a lesser extent in the intima; the latter very frequently shows irregularly thickened projections into the lumen. Often both the media and the intima are so involved that it is difficult to determine the limitations of the layers; a striking feature is the appearance of small muscle bundles surrounded and separated by enormously thickened connective tissue septums; at times even the individual muscle cells are thus surrounded and separated, the entire media in a preparation stained either by van Gieson's method or by Mallory's aniline blue method, having a striking alveolar appearance, resembling, architecturally, the isolated appearance of islets of hepatic parenchyma surrounded by connective tissue septums as in Laennec's cirrhosis of the liver.

Most frequently the entire circumference of the vein is involved, but occasionally (especially in advanced cases) there is a very pronounced irregularity of the fibrotic process, so that there seem to be localized bulgings into the lumen, and one part seems to be several times as thick as another (venofibrosis circumscripta s. nodosa). The lesions are equally pronounced in the vasa vasorum.

CLINICAL DATA

To begin with, we feel that there are several objections to the view that venosclerosis (fibrosis) is a process similar to arteriosclerosis.

9. Benda, C., in Henke and Lubarsch: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1924, vol. 2, pp. 829-833.

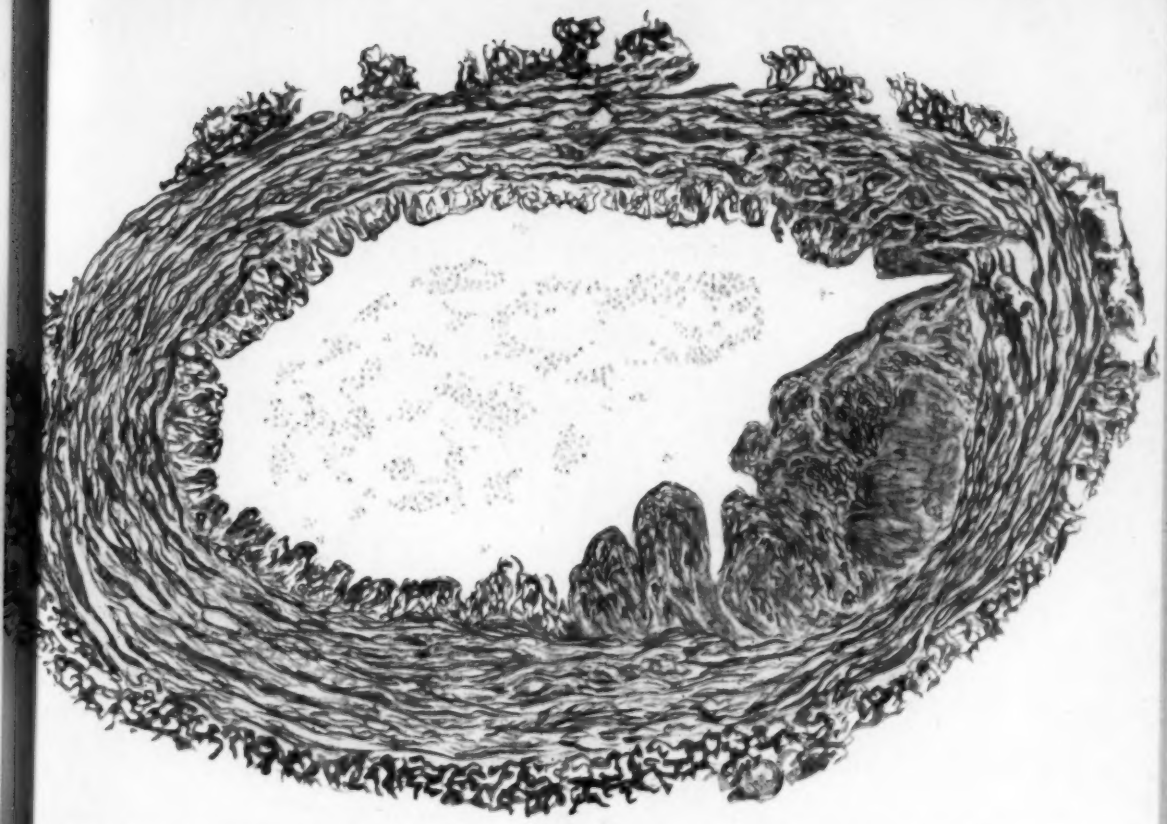

Fig. 1.—Circumscribed bulging of the wall of a vein, caused by marked local proliferation of fibrous connective tissue (venofibrosis circumscripta). The condition was observed in a case of gastric ulcer occurring in a man, aged 34. Mallory's aniline blue stain was used.

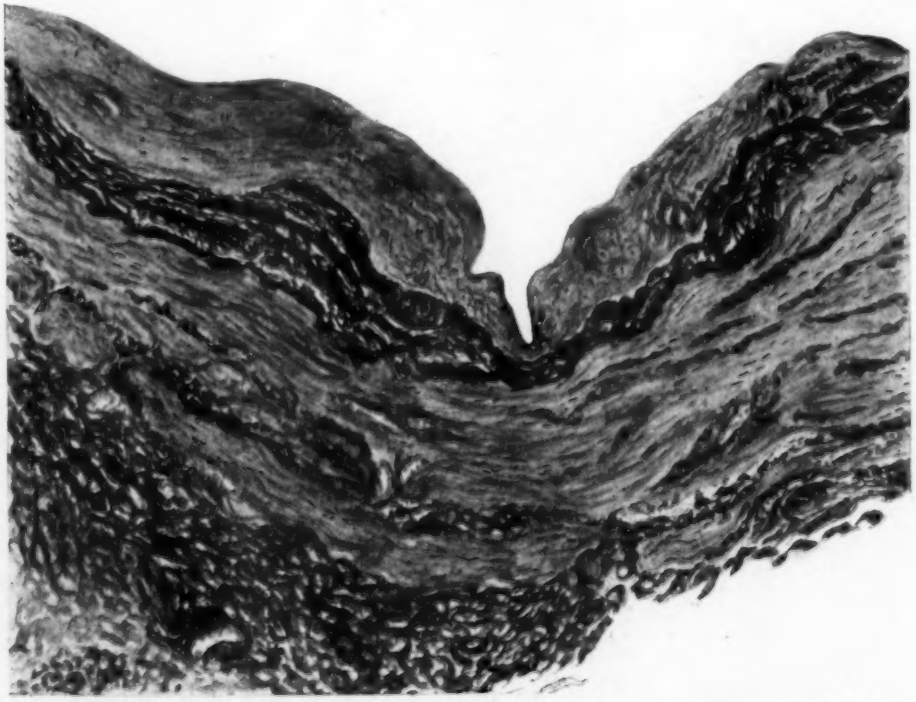

Fig. 2.—Thickened intima, uniformly structureless and denuded of endothelium; marked fibrosis between the thickened intima and the media. The condition was seen in a superficial vein of a leg in a case of duodenal ulcer, operated on ten years previously. Mallory's aniline blue stain was used.

Were the two processes similar or parallel to each other, venofibrosis should be met with much more frequently than it has been in the past. (In spite of our belief that the rarity of the condition is much more imaginary than real—a belief based both on previous experience and on the articles of Martin and Meakins and Martin and Tull—we consider that venofibrosis is rarer than arteriosclerosis, even allowing for the general oversight of the condition during the general physical examination. Who examines veins unless there are varicosities?) The patients observed by us, as well as by the author mentioned, were younger men—under 40 (Martin and Meakin's patients were largely under 30)—than those in whom diffuse arteriosclerosis is encountered. We have, however, found venofibrosis in three arteriosclerotic patients, one was a man aged 45, with a history of familial arteriosclerosis; and the other two were men aged 23 and 26, juvenile arteriosclerotic patients, one of whom had a family history of the condition. It is reasonable to suppose that were the two processes parallel (etiologically, as well as pathologically) veno(phlebo)fibrosis would have been observed particularly by some of the investigators (whose name is legion) who have produced arteriosclerosis artificially, whether by the mechanical method of Klotz or by feeding large amounts of cholesterol (Chalatow, Anitschkow, Saltykow) or of proteins (Newburgh and March, Nuzum and others). The histories of our patients do not point to lead, gout or syphilis, but frequently show an association with peptic ulcer. A few of our patients have been operated on for that condition, and, strange to say, these patients not only do not show any cardiac hypertrophy, but possess hearts demonstrably smaller than normal.

We believe venofibrosis is overlooked largely because it develops painlessly, slowly and insidiously, without edema (except in the cases of portal venofibrosis and thrombosis) and symptomlessly, unless inflammatory changes develop subsequently. Unless the veins are examined as methodically and regularly as are the arteries, venofibrosis will continue to be overlooked. It may be of interest to relate that since we called attention to our first two cases the house staff has repeatedly recognized the condition. *A priori* one should expect venous lesions to be much more common than arterial ones; thin-walled vessels, carrying from the tissues all their waste, as well as carbon dioxide, subjected to more mechanical strain, easily involved in injuries and inflammatory reactions—they seem to have escaped clinicopathologic studies.

We find venofibrosis a disseminated condition, present in superficial or deep parts of the body, never confined to one organ, to one extremity or to one side—in other words, venofibrosis has impressed us as a bilateral, symmetrical condition. The veins impart a sensation

of hard cords, small, mobile and smooth; their caliber is diminished—a sensation diametrically opposite to that offered by a varicose vein. When one is palpating a fibrosed vein near the malleoli, it is necessary to have the patient manipulate his foot—extending it and flexing it on the leg—in order to be sure that one's fingers are not feeling a tendon, so closely do the fibrosed veins and tendon simulate each other in the sensation they impart and in their color; a surgeon has exposed a fibrosed vein in performing biopsy and was uncertain, even then, whether the structure lying on his grooved director was a vein or a tendon.

A striking feature—usually the first to attract one's attention—is a longitudinal niche in the skin corresponding to the location of a fibrosed vein; this is particularly pronounced over a bone where the vein seems to groove the bone, and presents a depression along its entire course.

There are no subjective symptoms accompanying venofibrosis, not even when, as in one of our cases (of thrombo-angiitis obliterans), the vein of the "well" leg (i. e., as yet without symptoms) is actually fibrosed, thrombosed and canalized. Our study of a case of thrombo-angiitis obliterans has shown us that a superficial vein from the arm presented the usual characteristics of fibrosis; a superficial vein from the leg without any clinical abnormalities, subjective or objective, with normal oscillometric determination and normal reaction to the Aldrich test, was completely thrombosed, and the thrombus was canalized; neither the vein from the arm nor the vein from the well leg showed any inflammatory changes. We believe that our observation of the case not only confirms the prevalent opinion that thrombo-angiitis obliterans begins in the veins, but also suggests that the inflammatory process stressed by Buerger as the initial process may, in reality, be the terminal process, taking place only after the vessels have become thrombosed and devitalized.

SUMMARY

Venofibrosis (phlebosclerosis) is entirely different from arterio (athero)sclerosis, there being no evidence of fatty changes or of calcification; the entire process is apparently noninflammatory, and the histologic picture presents a varying degree of endothelial or subendothelial and medial replacement fibrosis.

The cases seen by us have invariably occurred in men under 40 years of age, none of them showing the slightest tendency to simulate—clinically—arterial lesions; a great majority of the patients had small hearts and low arterial tension; in other words, while venofibrosis may occur with arteriosclerosis, it is independent of it.

Venofibrosis is not rare, but is rarely recognized, because it is rarely looked for. The experience of Martin and Meakins, of Martin and Tull and of Widal and Bezançon testify to that effect. This lesion may indicate what Pende calls constitutional deficiency in the structure of the vascular wall. Most of our cases seem to be associated with peptic ulcers.

It is reasonable to assume that veins because of their weaker structure and greater exposure to injurious elements would be a more common site for lesions than the arteries.

Thrombo-angiitis obliterans begins in the veins, and the condition is not inflammatory; the inflammation associated with it is a terminal process occurring after the vessels have become thrombosed and devitalized.

OCCURRENCE OF NUMEROUS LARGE GIANT CELLS IN THE TONSILS AND PHARYNGEAL MUCOSA IN THE PRODROMAL STAGE OF MEASLES

REPORT OF FOUR CASES *

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The four cases of the prodromal stage of measles in which tonsillectomy was done reported in this paper showed extraordinary tonsillar pathologic changes; and as measles developed in all four of the patients within from one to five days after tonsillectomy, these pathologic changes may be reasonably ascribed to the measles. Further, the occurrence of measles was correctly predicted in three of the cases, based on the same changes as were found in the first case, in which typical measles developed two days after the tonsillectomy. Moreover, the pathologic observations on the tonsils in these four cases were the only observations of that type made on about 50,000 tonsils examined in this laboratory to the time of writing; also, as far as known, the four patients were the only ones in whom measles developed within a few days after tonsillectomy.

REPORT OF CASES

CASE 1.—C. T., a boy, aged 11, had frequent attacks of tonsillitis and sore throat, especially during the winter months. He breathed through his mouth. The clinical diagnosis was: septic tonsils and adenoids. Tonsillectomy was performed on Dec. 26, 1929. The tonsils were examined pathologically on Dec. 27, 1929. They showed marked lymphoid hyperplasia, hyperkeratosis and increase of stroma; they did not show tubercles. The most striking feature was the presence of great numbers of large giant cells in the germinal centers, and particularly beneath the epithelium of the crypts. At first it was thought that the condition was early Hodgkin's disease or malignant lymphoblastoma. A biopsy of one of the cervical glands was immediately carried out, but no giant cells were present in the gland, and no evidence of lymphoblastoma, the gland presenting the picture of simple lymphadenitis. Two days after the tonsillectomy the boy had a temperature of 102.5 F., coryza and mild conjunctivitis, with Koplik's spots on the mucous membrane of both cheeks. Two days later the fully developed eruption of measles was present. The recovery was uneventful.

CASE 2.—M. M., a boy, aged 4, had frequent attacks of tonsillitis and colds. There was chronic otitis media of the left side. The tonsils were enlarged. Adenoids were present. Tonsillectomy was performed on April 10, 1930. The

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† Dr. Warthin died on May 23, 1931.

tonsils showed marked lymphoid hyperplasia, hyperkeratosis, increase of stroma, with colonies of mouth organisms in crypts. No tubercles were found. In addition the tonsils presented the same extraordinary picture of numerous large giant cells in the germinal centers and beneath the epithelium of crypts, as well as in the mucosa between the epithelial cells. On the strength of the experience in case 1, inquiry was made as to the possibility of the child's having measles or having been exposed to measles with negative results. Three days later he presented coryza, conjunctivitis, Koplik's spots and fever. Two days later, he had a fully developed attack of measles.

CASE 3.—M. D., a girl, aged 8, had frequent attacks of bronchitis and tonsillitis. She had had otitis media every winter for four years. The clinical diag-

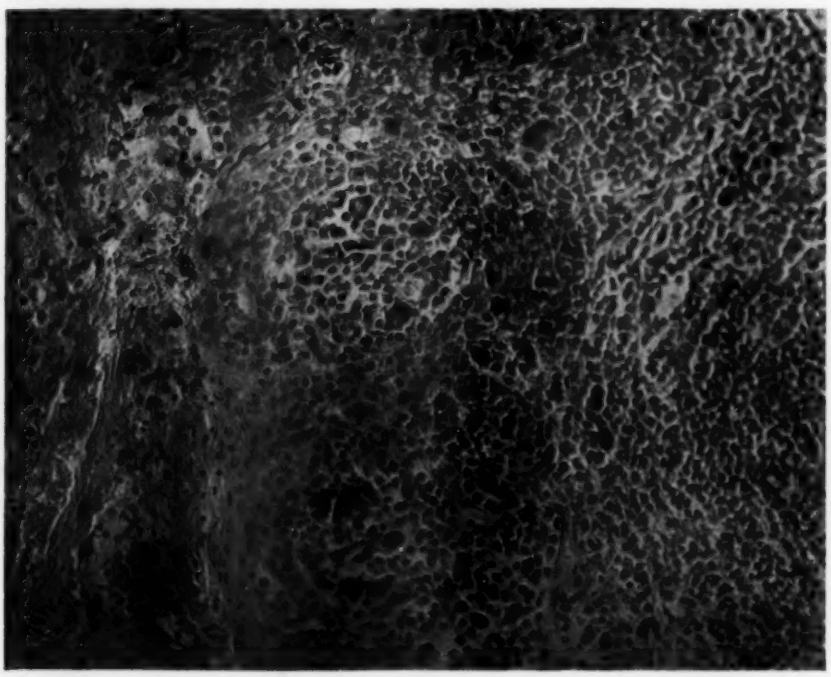

Fig. 1.—Low power view of the mucosa of a tonsil in case 2, removed five days before a fully developed attack of measles. Multinucleate giant cells are closely crowded in the subepithelial layer.

nosis was: septic tonsils and adenoids, with chronic otitis media of the left side. Tonsillectomy was performed on June 13, 1930. The tonsils showed lymphoid hyperplasia, hyperkeratosis, increase of stroma and colonies of mouth organisms in crypts. No tubercles were seen. In addition the tonsils presented the same picture of large giant cells in germinal centers and beneath and in the epithelium of the mucosa as in cases 1 and 2. A prediction of measles was made at once. Thirty-six hours after the operation the child began to have high fever, a blotchy maculopapular eruption and sore throat, with watery eyes. Koplik's spots were not present. After about thirty-six hours' duration, the rash began to fade slowly, and the temperature came down. There was a clinical difference of opinion as to

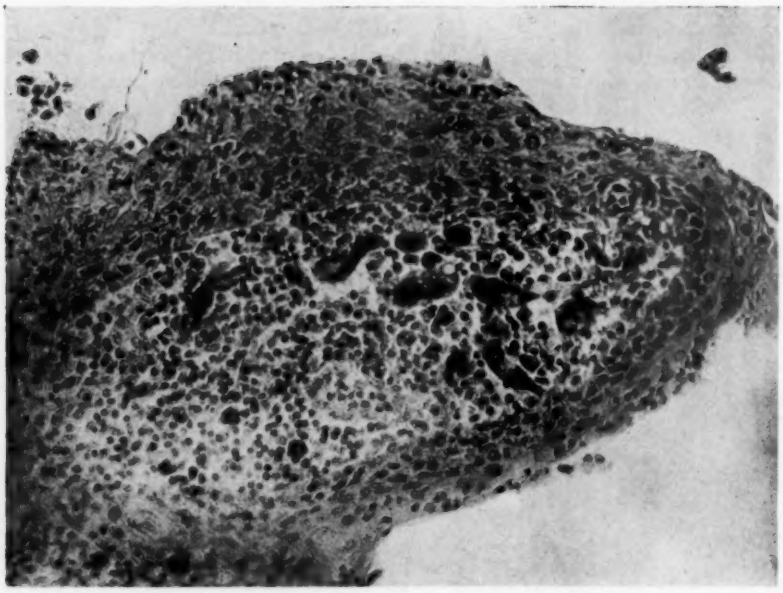

Fig. 2.—Higher power view of a portion of the mucosa of a crypt from a tonsil in case 2, showing the multinucleate giant cells beneath the epithelium.

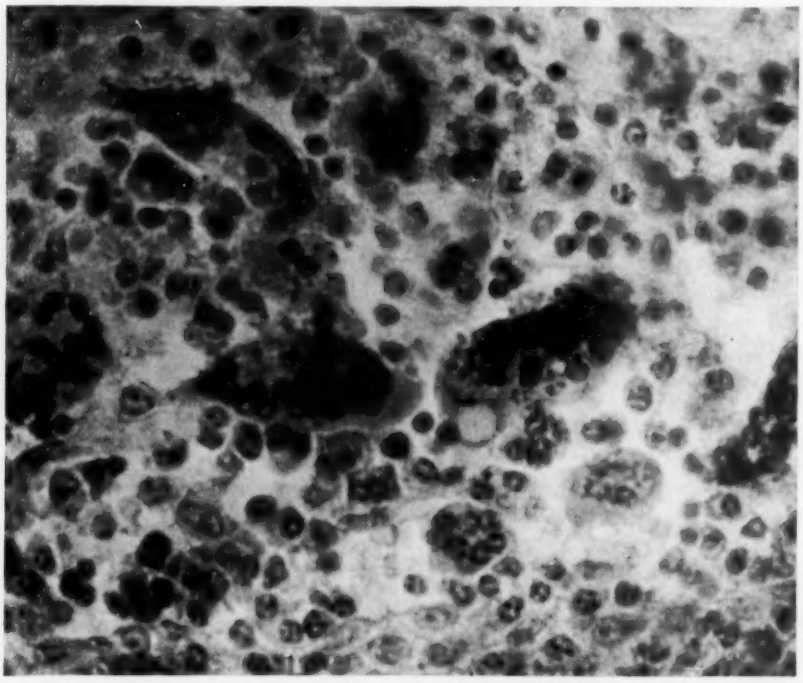

Fig. 3.—High power view of subepithelial giant cells in case 2. The round, granular nuclei are well shown.

whether or not the condition was measles, but this diagnosis was concurred in by the majority of the medical men who examined the patient.

Case 4.—Only one other pair of tonsils showing pathologic changes identical with those shown in cases 1, 2 and 3 had occurred in the tonsil material of this laboratory, aggregating about 50,000 cases, to the time of writing. In May, 1926, tonsils were received from St. Lawrence Hospital, in Lansing, Mich. These were from a girl, B. C., a patient of Dr. A. E. Owen. The pathologic diagnosis returned was: "Marked lymphoid hyperplasia with marked exhaustion of germinal centers and many atypical lymphoblasts. Giant cells and cells of myeloid type. This child must have some severe systemic process. Is there a general swelling

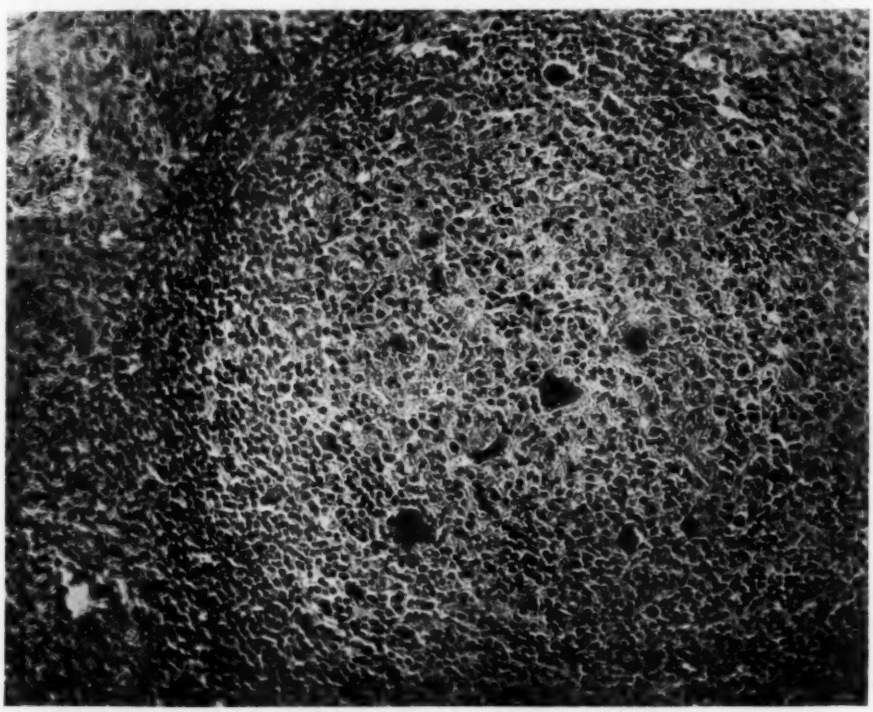

Fig. 4.—Germinal center from a tonsil in case 2, showing the lymphoid exhaustion of the center, the prominence of the lymphoblasts and numerous multinucleated giant cells in various stages of formation. A superficial resemblance to Hodgkin's disease is suggested.

of lymph nodes? Has the child had infectious mononucleosis? What is the blood count? Please give us history." No answer to these inquiries was received. After the tonsils in the other three cases had been examined in the laboratory a positive diagnosis of measles was made in this case, and a letter was written to Dr. Owen, asking whether his patient had not had measles following the tonsillectomy. In his reply of Oct. 6, 1930, Dr. Owen wrote: "In reply to your inquiry, beg to advise that this patient did have measles, developing the day following operation." This made the third case in which the prediction of measles based on the pathologic observations in the tonsils was confirmed.

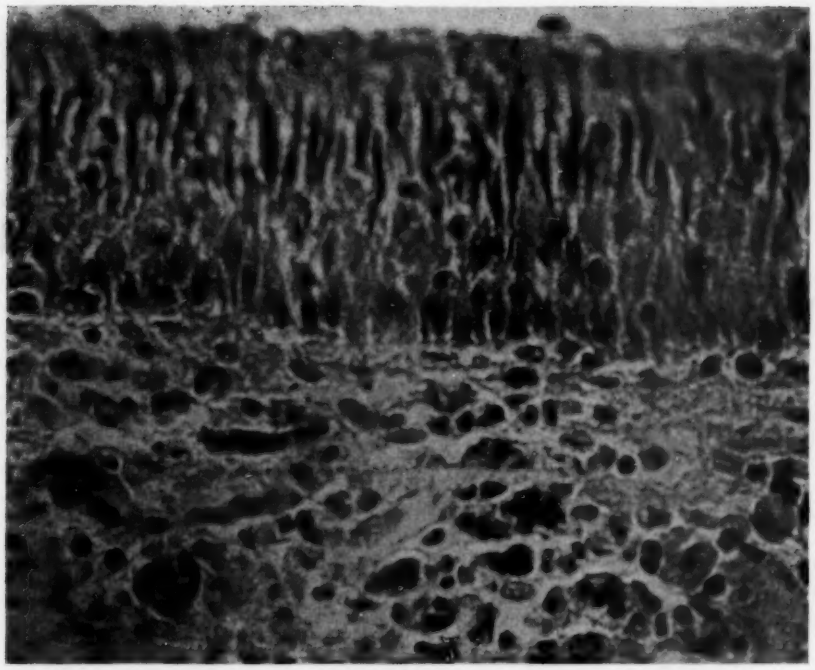

Fig. 5.—Mucous membrane from the nasopharynx in case 2, showing subepithelial formation and infiltration by multinucleate giant cells.

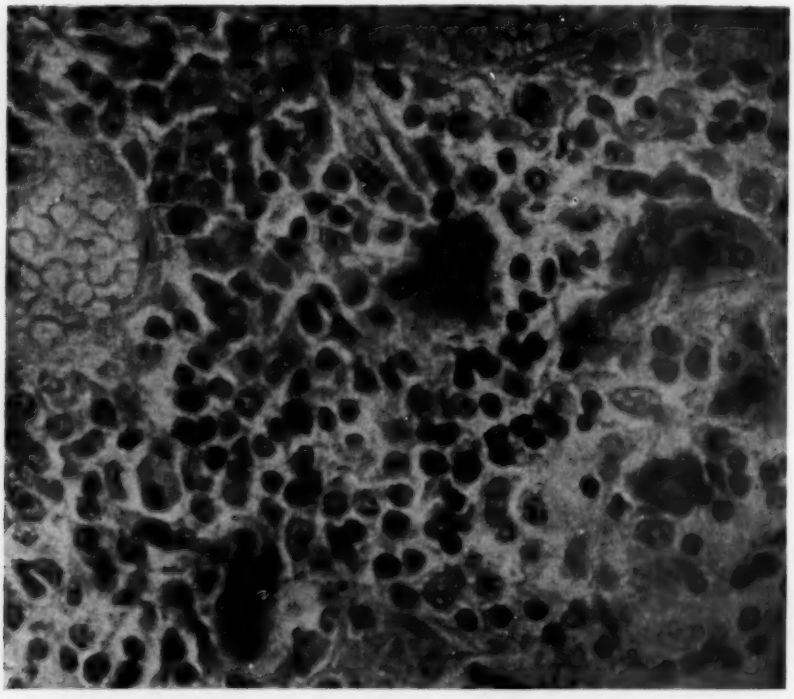

Fig. 6.—Multinucleate giant cells in subepithelial lymphoid tissue of a tonsil in case 2. Two congested capillaries are shown in part. Note the noninvolvement of the vascular endothelium.

Pathologic Observations in Cases 1 to 4—The tonsils and adenoids in the four cases of the prodromal stage of measles in which tonsillectomy was done all showed the same pathologic features: Beneath the epithelium of the tonsillar surface and crypts, there was a narrow zone filled with large, syncytial, multinucleate giant cells. They were round or irregularly lobed. They showed no peripheral arrangement of the nuclei. No cells of the Langhans type were seen. The nuclei were arranged in a grapelike cluster in the center of the cell. They were granular and stained lightly with hematoxylin. Similar cells were found in the mucosa between the epithelial cells, and also in the germinal centers. There were a few in the lymphoid tissue between the germ centers. The giant cells varied greatly in size and in the number

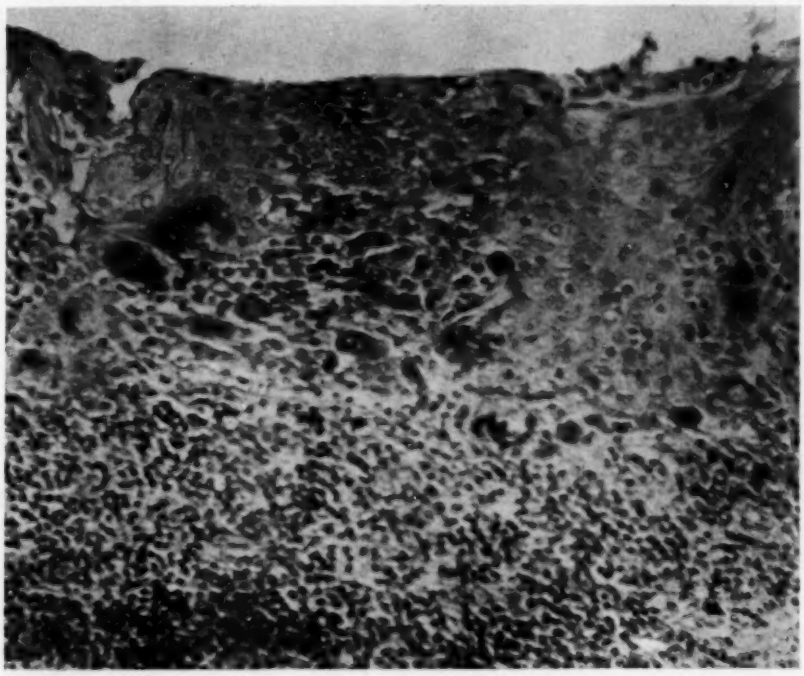

Fig. 7.—Low power view of tonsillar mucosa in case 4, showing the numerous subepithelial multinucleate giant cells.

of nuclei, although the majority were large, many of them averaging about 100 microns. There were some with as many as from 70 to 100 nuclei. The largest had a rather scanty cytoplasm that stained bright red with eosin. In these large forms the nuclei were often pyknotic and fragmented. One received a definite impression that the giant cells arose by amitotic division in hyperchromatic cells resembling lymphocytes in the subepithelial reticulo-endothelial layer and in the germinal centers, and wandered toward and into the mucosal epithelium. In the latter there were numerous elongated forms between the epithelial cells, with their long axes toward the surface. All possible transition stages of development from the hyperchromatic lymphocyte form to the largest multinucleated giant cells were present. The great majority of these showed nuclei in various stages of karyor-

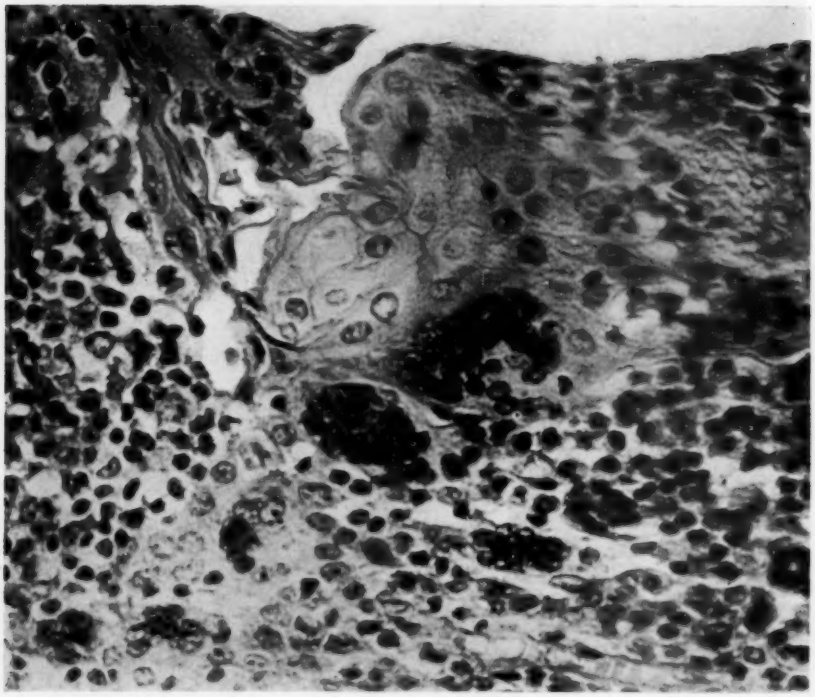

Fig. 8.—Higher power view of the tissue shown in figure 4, showing the characteristic clustered nuclei of the subepithelial giant cells.

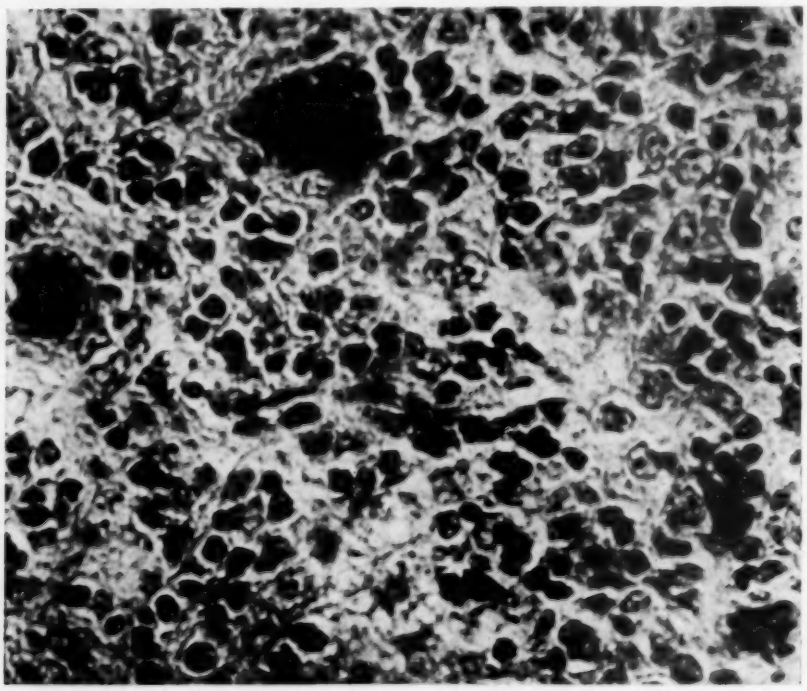

Fig. 9.—Large multinucleated giant cells in subepithelial lymphoid tissue of tonsils in case 4.

rhexis and pyknosis. The low power view of these tonsils presented a striking picture, as the epithelium of the surface and of the crypts was outlined by a zone of giant cells. Aside from the giant cells the tonsils presented little change varying from that of the ordinary enlarged tonsil. The germinal centers, particularly those near the epithelial surfaces, showed a marked lymphoid exhaustion, with large, pale, swollen, maternal lymphoblasts and giant cells. The blood vessels near the surface were congested, and there was occasionally a minute hemorrhage where the giant cells were aggregated in the largest number. There was no evidence of any of the giant cells arising from the vascular endothelium. No cell inclusions were found in the latter. The pharyngeal mucosa from the adenoids in these four cases showed precisely similar pathologic changes.

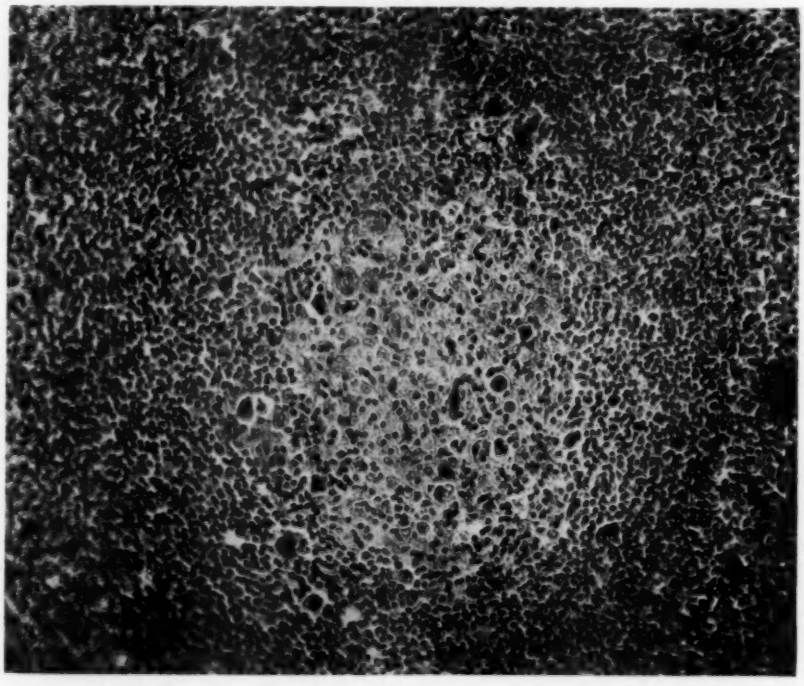

Fig. 10.—Germinal center from a tonsil in case 4, showing characteristic lymphoid exhaustion, prominence of lymphoblasts and various stages of formation of multinucleate giant cells.

COMMENT

The interpretation of these changes can be only that they are detensive. In the giant cells is most probably to be found the etiologic agent of measles. Nevertheless, staining with diverse bacteriologic technical methods failed to reveal any intracellular micro-organisms or inclusions in any way resembling parasites. In all four cases, however, the tonsillar tissues contained great numbers of a shortchained streptococcus, the individual cocci being slightly oval in form. No spirochetes

or spirilla could be demonstrated by the silver impregnation methods. No evidence of phagocytosis of the streptococci by the giant cells could be obtained.

The tonsils in these four cases present a unique pathology not seen in any other instance in the tonsils of 50,000 patients that have been examined in this laboratory. Nor do the records show that there was any other prodromal case of measles in this material. It, therefore, seems reasonable to connect this pathology with the measles. I feel confident that these changes represent the essential pathology of measles in the upper part of the respiratory tract, and that these giant cells must be phagocytic for the etiologic agent of measles, whatever this may be. I regret the inability to demonstrate this agent. Nearly 50 special staining methods for the demonstration of micro-organisms in tissues have been tried out on sections from these four cases, but without success. This effort will be continued, however, in the hope that something may be found.

Very little has been written on the pathology of the mucous membrane in measles. In 1909, Ewing [1] made a summary of the small number of observations published to that time on the pathologic changes in the skin and mucous membrane in measles, and made some additions. In his conclusion, he made the following statement regarding the cell changes in the mucous membrane:

> If there is anything specific in these lesions of the mucous membranes it is the extensive subepithelial infiltration with round cells, which often shows a focal distribution, and the focal necroses, and it has seemed to me that the occurrence of the former probably determines the latter lesion in skin, pharynx, and respiratory tract. Koplik's spots seem to be one expression of this focal character of the process. . . . There is a uniformity in the number of large round cells in the derma, and these seem to be divided among exuded large mononuclear leukocytes and multiplying endothelia.

In 1920, Mallory and Medlar [2] reported a study of the cutaneous lesions in measles. Their material was derived almost wholly from the skin of adult patients showing the fully developed eruption of measles. Buccal mucous membrane containing Koplik's spots was excised from six patients from forty-eight hours before to twenty-four hours after the appearance of the exanthem. These lesions were described as follows:

> Microscopically the lesions consist of an exudation of serum and endothelial leucocytes into the stratified epithelium where they usually collect near its outer surface. The epithelial cells in the infiltrated focus undergo necrosis, and the

1. Ewing, James: J. Infect. Dis. **6**:1, 1909.
2. Mallory, F. B., and Medlar, E. M.: J. M. Research **41**:327, 1920.

leucocytes may collect together so as to form minute pustules. In addition there are retrograde changes in the epithelial cells such as direct division of the nuclei and the formation of granules and globules with basic and acid staining properties. The lesion is exactly like that in the epidermis covering the skin lesions, and corresponds with it in the time of its appearance, but instead of drying up the tissue involved tends to macerate so that slight erosions are formed which may become secondarily infected by organisms present in the mouth, and thus enlarge into shallow or more or less extensive ulcerations.

It will be noted, from the statements quoted that neither Ewing nor Mallory noted the occurrence of multinucleate syncytial giant cells in the lesions of the mucous membrane in measles. Nor do the illustrations by Mallory of the histology of the Koplik spots from the buccal mucous membrane show any indication of their presence. In measles either there is a difference in the pathology of the lesion in the mucous membranes of tonsil and pharynx from that of the buccal mucosa, or these investigators missed what is to my mind the most striking feature of the lesion in the tonsil and pharyngeal mucosa. It seems most probable that they failed to recognize it. Further, no participation of the vascular endothelium in the production of the giant cells was seen in the four cases herein described. The blood vessels were congested, but the endothelium appeared unaltered. No cell inclusions, as described by Mallory, were seen in the endothelium. No focal necroses were observed, but this may have been due to the early nature of these lesions, which were prodromal to the exanthem. Certain aggregations of the giant cells, with greater localized congestion and edema, suggested potential Koplik's spots. In the case in which the exanthem appeared on the day after the tonsillectomy, a greater number of degenerating giant cells were found in the mucosa, between the epithelial cells and even on their surface.

CONCLUSION

The essential pathologic lesion in the tonsils and pharyngeal mucosa in the prodromal stage of measles (from twenty-four to ninety-six hours before the exanthem) is a subepithelial infiltration of multinucleate syncytial giant cells, lymphocytes and monocytes, wandering of the giant cells into the mucosa and on to its surface, with edema and congestion, marked lymphoid exhaustion of the germinal centers with production of the multinucleate giant cells from cells of the lymphoblast type and migration of these cells toward the mucosa. Local aggregations of the giant cells, with more marked local edema and congestion, suggest potential Koplik spots. This pathology is so distinctive that a positive diagnosis of measles may be made from one to five days before the exanthem appears. The process is interpreted as a

defensive one, directed to an etiologic agent, either in or on the pharyngeal mucosa. This bears out the view of a primary respiratory infection. No evidence of phagocytosis by these giant cells could be obtained by the use of a large number of staining methods applicable to the demonstration of micro-organisms. No participation in the process by the vascular endothelium was noted, nor could any inclusions be found in the latter.

INTRADURAL TERATOID TUMORS OF THE SPINAL CORD

REPORT OF A CASE *

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Bidermal, or teratoid, tumors of the spinal cord are exceedingly rare. I have not been able to find a single case of genuine tridermal or teratomatous new growth of the spinal cord recorded in the literature. In 1888, Gowers and Horsley [1] collected 58 cases of tumors of the spinal cord. In 1895, Starr [2] found 123 cases reported. No mention of teratoma or of teratoid tumors was made in these two papers. Schlesinger's monograph [3] on 400 collected cases included one of intramedullary and one of extradural teratoma. The 70 cases of tumors of the spinal cord collected by Collins [4] in 1902 and the 141 by Stursberg [5] in 1908 included none of teratoma. There was 1 case of teratoma in Flatau's [6] series of 213. Frazier and Allen [7] and Steinke [8] found 1 case of extradural, extramedullary teratoma among the 330 in which operation was performed. Lennep [9] discussed the 153 cases of spinal tumors in which operation was performed, which he found in the literature from 1908 to 1920. No teratoma was mentioned. In Clymer, Mixter and Mella's experience [10] with 52 cases of tumors of the spinal cord during an interval of ten years, a teratoma was not found. Among

* Submitted for publication, Nov. 8, 1930.

* From the Department of Pathology, Albany Medical College, and the Pathological Laboratory of the Albany Hospital.

1. Gowers, W. R., and Horsley, V.: Tr. Med.-Chir. Soc. **71**:377, 1888.
2. Starr, M. A.: Am. J. M. Sc. **109**:613, 1895.
3. Schlesinger, H.: Beiträge zur Klinik der Rückenmarks- und Wirbeltumoren, Jena, Gustav Fischer, 1898.
4. Collins, J.: M. Rec. **62**:882, 1902.
5. Stursberg, H.: Centralbl. f. d. Grenzgeb. d. Med. u. Chir. **11**:91, 141, 185, 225 and 277, 1908.
6. Flatau, E., in Lewandowsky, M.: Handbuch der Neurologie, ed. 7, Berlin, S. Karger, 1911, vol. 2, p. 616.
7. Frazier, C. H., and Allen, A. R.: Surgery of the Spine and Spinal Cord, New York, D. Appleton & Company, 1918, chapt. 8, p. 498.
8. Steinke, C. R.: J. Nerv. & Ment. Dis. **47**:418, 1918.
9. von Lennep, H.: Deutsche Ztschr. f. Chir. **160**:136, 1930.
10. Clymer, G.; Mixter, W. J., and Mella, H.: Proc. Boston Soc. Psychiat. & Neurol., Nov. 18, 1920; J. Nerv. & Ment. Dis. **53**:229, 1921.

the 100 verified tumors of the spinal cord reported by Elsberg,[11] no teratoma was listed. Elsberg and Constable[12] recently analyzed 45 cases of lesions of the cauda equina, which did not include a teratoma. Those complex tumors of the spinal cord listed as teratomas in the literature have turned out to be teratoid, or bidermal, on personal study of the microscopic descriptions of the recorded cases.

The case of teratoid tumor of the spinal cord here presented occurred in the medical service of Dr. Thomas Ordway and the neurosurgical service of Dr. Arthur H. Stein of the Albany Hospital, both of whom provided me with the details of the clinical history of the patient.

REPORT OF CASE

History.—R. S., 24 years old, married, a toolmaker, was seen by Dr. Thomas Ordway in consultation with Dr. Charles K. Burt, in Lake George, N. Y., on Aug. 18, 1922. As a child, he had whooping cough and measles. There was a vague history that for a short time he could not walk, although previously he had been able to do so. The exact nature of this difficulty was never known, but when he tried to enter the army in 1917, it was said that the old trouble was probably the result of infantile paralysis. His family history was not important.

He had been working in the "tests" at the General Electric Company at Schenectady until two weeks before, when he felt a pain in the back in the lumbar region. This was believed to be "rheumatism," for which he was treated during the next few days.

During the week before admission, he had gradually become worse and the pain in the back more intense. A slight, inconstant insecurity of the legs developed. He continued to work until six days before admission, when pains in the legs developed. He went to a mechanotherapist, who applied electricity. Gradually, both lower extremities became so much weaker that he was unable to drive his car.

During the last twenty-four hours, the patient had been in bed and could hardly move his legs. The pain in the back continued. Early in the morning he was unable to pass urine and had to be catheterized. The bowels did not move, and the patient could not even expel the water given by enema. He had repeated spells of vomiting. The pain in the back became severe and was only slightly relieved by hypodermic injections of morphine.

Physical Examination.—Physical examination disclosed a well developed, well nourished young man lying in the dorsal decubitus, rather nervous and worried. The skin was somewhat dry. There was a pilonidal cyst in the sacral region. His pupils were equal and reacted normally. There was no demonstrable defect of the cranial nerves. A slight rigidity of the neck was present. The temperature was 101, and the pulse rate, 80. There was no gross disorder of sensation, although there was some retardation of localization in the legs and the lower part of the trunk. There were numbness and paresthesias of the legs and intense pain in the back. The umbilical and cremasteric reflexes were present. The knee jerks were markedly exaggerated. The patellar twitch was elicited. There was a slight

11. Elsberg, C. A.: Tumors of the Spinal Cord, New York, Paul B. Hoeber, 1925; Diagnosis and Treatment of Surgical Diseases of the Spinal Cord and Its Membranes, Philadelphia, W. B. Saunders Company, 1916.

12. Elsberg, C. A., and Constable, K.: Arch. Neurol. & Psychiat. **23**:79, 1930.

suggestion of a Babinski sign on the left. There was a bilateral positive Kernig sign. The back was rigid. The muscles were stiff and firm. There had been no convulsions or twitchings. The condition suggested myelitis of the lumbar cord.

Roentgen Examination.—The patient was moved to the Albany Hospital, Albany, N. Y., on Aug. 19, 1922, for roentgen examination of the spine. The roentgenograms showed a failure of union of the neural arch of the fifth lumbar vertebra and the first sacral segment suggesting spina bifida occulta. The spine was angulated at the twelfth dorsal vertebra, and the right psoas muscle appeared to be in a state of contraction.

Laboratory Examination.—The spinal fluid showed intense xanthochromia. The Pandy test for globulin gave a markedly positive reaction. The cell count

Fig. 1.—A drawing of an intradural teratoid tumor of the spinal cord. The dura is reflected to show the general character of the tumor, which was an intimate connection with the posterior aspect of the spinal cord. Note the congested blood vessels coursing over the tumor. The tumor is shown in its natural size. The drawing was loaned by Drs. Thomas Ordway and Arthur H. Stein.

was 2 cells per cubic millimeter. The Wassermann tests on the spinal fluid and blood gave negative results.

Course.—There was disturbed sensitivity to heat, cold and pin prick on the soles of the feet, extending in a diminishing degree up the left leg. The patient had almost complete paralysis of the legs, particularly of the left. After a few days, he was able to move the right leg again fairly well, but could flex and

abduct the left only slightly. He could also expel the enema fluid, so that it did not have to be siphoned off. The retention of urine continued, however. In spite of great care in catheterization, cystitis developed.

Operation was performed by Dr. Arthur H. Stein on Sept. 16, 1922, and an intradural tumor of the spinal cord was found at the level of the second and third lumbar vertebrae (fig. 1). On the right, it was intimately connected with the cord itself. On the left, it was somewhat separated from, but pressed deeply on, the cord. A small specimen from this left side was taken for microscopic examination. Evidence of a considerable amount of old hemorrhage was found within the spinal canal. As the tumor could not all be removed, a decompression of the growth at the level of the first, second and third lumbar vertebrae was done

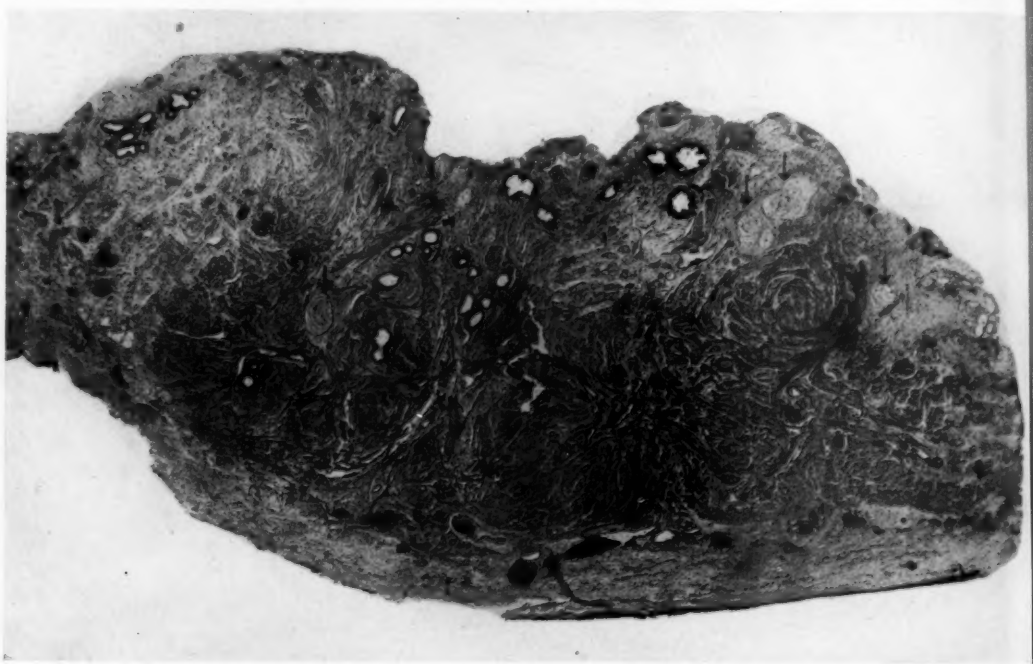

Fig. 2.—A photomicrograph showing the general distribution of the glandular elements among the smooth muscle bundles. The pacinian corpuscles are indicated by arrows. A few fat cells are present. Hematoxylin and eosin; × 30.

to relieve pressure. It was hoped that the tumor might be extruded, and that this might result in improvement in the function of the cord.

There was considerable shock following the operation. The pulse rose to around 135 and was weak and irregular. The color was poor, and there was an elevation of temperature to 101 F. for a few days.

By Oct. 26, 1922, the patient was gradually gaining strength. The annoying, persistent pain, which had so disturbed his sleep, had disappeared. After some time in a wheel chair, he was able to take a few steps. The function of the bladder improved, although there was not yet complete control of the bladder and rectum.

On November 13, the patient was up for a short time. At this time, it was thought that it was better for him to go about with a couple of chairs rather than on crutches, as he was very insecure on his feet.

On November 23, a letter from his physician stated that the patient was able to walk well with crutches. He was rapidly improving, but still had incontinence of urine.

He was gradually able to get about without crutches. His general condition was satisfactory.

Fig. 3.—A photomicrograph showing the well formed pacinian corpuscles. The tall columnar cells lining the glands form finger-like projections into the lumen. Many smooth muscle fibers are present in the right half of the section. Numerous thin-walled vascular channels are seen. Hematoxylin and eosin; × 119.

On July 22, 1930, the patient wrote a letter to Dr. Ordway, stating that he was still with the General Electric Company, was feeling well, and could drive his car again. However, as some dribbling of urine continued, he had to wear a urinal all the time. He was annoyed most by the constant drainage from trophic ulcers on his feet.

Microscopic Examination of Tumor.—Block serial sections, cut from the entire specimen that was removed for biopsy, were stained with hematoxylin and eosin,

Mallory's eosin and methylene blue, aniline blue, phosphotungstic acid and hematoxylin, Perl's prussian blue iron method and the silver impregnation method of Hasegawa.[13]

A rather compact, but apparently purposeless, arrangement of bundles of smooth muscle fibers made up the bulk of the various sections. The muscle bundles were separated by thin strands of dense collagen. A few fat cells were present here and there. A number of pacinian corpuscles and nerve trunks were embedded between the muscle fibers. These tactile corpuscles were well formed (fig. 2).

Glands, occurring singly and in small groups, were distributed throughout the sections. All of these glandular structures were lined with both ciliated and nonciliated epithelia, supported by a single layer of flat basement cells. The large spheroid or ovoid nucleus was generally located nearer the inner border of the cell. The lumina of the smaller glands appeared round or oval, and were lined by cuboidal cells. The larger glands were irregular in shape. The lining epithelium here varied from cuboidal to tall columnar and formed finger-like projections into the lumen. A closer study of the lining cells under high power showed that the free borders of the individual cells were not uniformly even. The free border of some of the cells extended farther out into the lumen, like little pseudopods. Most of the lining cells contained varying amounts of finely granular, yellowish pigment in their cytoplasm. This pigment did not give a positive prussian blue reaction for iron. However, that iron was present in some of these cells was evidenced by the presence of fine, blue, dustlike particles. These yellowish granules did not reduce an ammoniacal solution of silver after the method of Hasegawa; in other words, the pigment granules were not argentaffine. In sections stained with phosphotungstic acid and hematoxylin, none of these cells contained blepharoplasten along the free borders, so that the glandular structures were probably not of ependymal origin. Some of the structures suggested sweat glands or the glandular tissue of the breast or of the prostate (fig. 3).

COMMENT

In a previous paper,[14] teratomas and teratoid tumors of the brain were discussed. Compared with the hundreds of other tumors of the brain and of the spinal cord reported, those developing from multipotential or totipotential cells are rare. Many of the structures found in these complex tumors are often difficult to classify, owing to the frequently undifferentiated or abortive character of the derivatives of the three primitive germ layers. Frequently, too, the ectodermal and mesodermal elements tend to overgrow at the expense of the endodermal elements, which may either become retarded in their growth or disappear entirely. For this reason, it may be extremely difficult to judge whether a tumor under consideration is of multipotential origin (teratoid) or of totipotential origin (teratomatous).

These teratoid tumors are obviously congenital. They are often associated with other congenital abnormalities or defects. One of the

13. Hasegawa, T.: Virchows Arch. f. path. Anat. **244-245**:8, 1923.

14. Hosoi, K.: Arch. Path. **9**:1207, 1930.

cases of Kubie and Fulton [15] and the case here reported showed spina bifida occulta and a pilonidal cyst. Hansmann's [16] case was a veritable pot-pourri of congenital defects. There was an associated syringomyelia in the cases of Gerlach,[17] André-Thomas and Quercy [18] and Bielschowsky and Unger.[19]

It may not be amiss to mention here the few recorded cases of extradural, intravertebral teratoid or teratomatous tumors. Virchow [20] described an extradural, intravertebral tumor composed of fibrous connective tissue, fat and cartilage. In Brun's [21] case, an extradural growth surrounded the cord for a considerable distance in the form of a cylindric jacket. In their review of 330 collected cases of spinal tumors in which operation was performed, Frazier and Allen [7] mentioned an extradural, extramedullary tumor in the lumbosacral region in a man between 30 and 39 years of age.

The table shows that three of the ten cases occurred in childhood.

Since these complex tumors are benign and grow slowly over a period of many years, the acute symptoms of pressure on the spinal cord may not arise until in adult life. In the case here reported, it is to be noted that this young man gave a vague history of not being able to walk for a short time when a child, although previously he had been able to do so. The clinical aspects of spinal tumors have already been discussed exhaustively in the various excellent monographs referred to.

As regards sex, the tumors occurred in five males and three females. Though this series of cases of tumors of the spinal cord is too small to be of any significance, it is interesting to note that similarly both the teratomatous and the teratoid tumors of the brain more frequently affected the male sex.

Histologically, only the derivatives of the mesodermal elements were present in the cases of Gowers,[22] Gerlach [17] and Forbes.[23] Frick [24]

15. Kubie, L. S., and Fulton, J. F.: Surg. Gynec. Obst. **47**:297, 1928.

16. Hansmann, G. H.: Surg. Gynec. Obst. **42**:124, 1926.

17. Gerlach, W.: Deutsche Ztschr. f. Nervenh. **5**:271, 1894.

18. André-Thomas and Quercy: Nouvelle icon. de la Salpêtière **25**:364, 1912.

19. Bielschowsky, M., and Unger, E.: J. f. Psychol. u. Neurol. **25**:173, 1920.

20. Virchow, R.: Die krankhaften Geschwülste, Berlin, A. Hirschwald, 1863, vol. 1, p. 514.

21. Bruns, L.: Rückenmarkstumoren, in Eulenberg, A.: Encyclopädische Jahrbücher der gesammten Heilkunde, Fünfter Jahrgang, Leipzig, Urban & Schwarzenberg, 1895, p. 533; Die Geschwülste des Nervensystems, Eine klinische Studie, Berlin, S. Karger, 1897, p. 274.

22. Gowers, W. R.: Tr. Path. Soc. London **27**:19, 1876.

23. Forbes, J. G.: St. Barth. Hosp. Rep. **41**:221, 1905.

24. Frick, K.: Frankfurt. Ztschr. f. Path. **7**:127, 1911.

Reported Cases of Teratoid Tumors of the Spinal Cord

No.	Author	Sex	Age, Years	Location	Size	Ectodermal Structures	Mesodermal Structures	Structures Hard to Classify
1.	Gowers, 1876	..	Adult	Conus medullaris	0.5 by 0.5 by 0.4 in.	.....	Connective tissue, striated muscle, fat	.....
2.	Gerlach, 1894	M	36	Upper cervical	About 3 mm. long	.....	Connective tissue, primitive and adult muscle fibers, cartilage	Embryonal tissue
3.	Forbes, 1905	M	5.5	Midcervical	Size of haricot bean	.....	Cellular connective tissue, embryonal and adult striated muscles, fat cells, multinucleated giant cells (osteoclasts ?)	.....
4.	Frick, 1911	F	41	2d to 5th lumbar vertebrae	.....	Numerous blond hairs	Connective tissue, bone with myeloid tissue in marrow, fat	.....
5.	André-Thomas and Querey, 1912.	..	..	Cervical and dorsal cord	.....	Ependymal cells, glial elements (glioma)	Connective tissue, striated muscle, numerous blood vessels	.....
6.	Bielschowsky and Unger, 1920	M	37	3d cervical segment	Twice walnut size	Fine hairs	Connective tissue, fat cells, endothelioma or alveolar sarcoma	.....
7.	Hansmann, 1926	F	21 days	Sacral	6 cm. diameter	Stratified squamous epithelium, nerves, glia cells, ependyma, ependymal glioma (?)	Myxomatous connective tissue, smooth muscle, cartilage, fat, lymphoid cells	Cysts lined with high columnar cells
8.	Kubie and Fulton, 1928	M	2	9th dorsal to 1st lumbar	6 by 1.5 cm.	Mucous and serous glands, large myelinated nerve fibers	Connective tissue, smooth muscle	Cysts lined with ciliated columnar cells
9.	Kubie and Fulton, 1928	F	27	3d and 4th cervical	.....	Mucous and serous glands, myelinated nerve fibers, ganglion cells (?)	Connective tissue, smooth muscle, fat, cartilage, lymphoid tissue	Cysts lined with ciliated cuboidal to columnar cells
10.	Hosoi, 1930	M	24	2d and 3d lumbar	About 1.5 by 3.5 cm.	Nerve fibers, pacinian corpuscles	Connective tissue, smooth muscle, fat cells	Glands lined with ciliated and nonciliated columnar cells

described a teratoid tumor containing bone with myeloid reaction in the marrow spaces. It is difficult to say just what is the nature of the cysts or glands lined by ciliated and nonciliated, tall columnar cells. In two of the reported cases there were an associated glioma and an endothelioma or alveolar sarcoma. Endodermal elements were uniformly lacking, so that all of the collected complex tumors of the spinal cord are bidermal. Intradural tridermal tumors or genuine teratomas are perhaps yet to be described.

SUMMARY

Complex tumors of the spinal cord are of extreme rarity. Nine cases are recorded among the hundreds of reported tumors of the spinal cord. An additional case of teratoid tumor of the lumbar spinal cord in a young man, who had spina bifida occulta and a pilonidal cyst, is here reported. Owing to early spinal decompression, he regained the use of both of his lower extremities. Only a slight incontinence of urine was left.

RUPTURED ANEURYSM OF THE CYSTIC ARTERY OF THE GALLBLADDER AS A RESULT OF TOXIC ARTERITIS

REPORT OF A CASE *

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Judged from the literature, aneurysm of the cystic artery is rare. Four cases have thus far been reported. Its interest, however, lies, not in its rarity, but rather in the mechanism of its formation.

In 1883, Chiari [1] reported a case of multiple (two) aneurysms of the cystic artery associated with ulcerative cholecystitis and cholelithiasis. One of the aneurysms had ruptured as a result of the irritation of a passing stone. On microscopic examination, he found that the media and the adventitia of the vessel had been eroded by an ulcer, and that the intima had herniated through to form a true aneurysm.

In 1917, Klotz [2] described a case of multiple aneurysms of the cystic and hepatic arteries. The underlying cause was a generalized periarteritis nodosa. Microscopically, he found a perivascular accumulation of lymphocytes and leukocytes, with an accompanying hyaline degeneration of the media. The intima and the outer coats were secondarily involved by the inflammatory process. The same author described a second case similar to the first, except that the aneurysmal involvement was limited to the hepatic artery.

In 1920, Högler [3] reported a case of aneurysm of the cystic artery in which rupture had occurred into the cystic duct. Microscopically, atherosclerotic changes were present in the vessel. The aorta and the celiac artery were similarly involved.

Walter's [4] case of periarteritis nodosa, described in 1921, was similar to that of Klotz.

Aneurysms of the hepatic artery are more common. In 1923, Friedenwald and Tannenbaum [5] gathered 65 cases (including one

* Submitted for publication, Oct. 14, 1930.

* From the Department of Pathology of Cook County Hospital, Richard H. Jaffé, Director.

1. Chiari, H.: Berstung eines Aneurysmas der Arteria cystica in die Gallenblase mit tödlicher Blutung, Prag. med. Wchnschr. **8**:33, 1883.

2. Klotz, O.: Periarteritis Nodosa, J. M. Research **37**:1, 1917.

3. Högler, F.: Beitrag zur Klinik des Leber und Milzarterien Aneurysmas, Wien. Arch. f. inn. Med. **1**:509, 1920.

4. Walter, H.: Periarteriitis nodosa, Frankfurt. Ztschr. f. Path. **25**:306, 1921.

5. Friedenwald, J., and Tannenbaum, K. H.: Aneurysm of the Hepatic Artery, Am. J. M. Sc. **165**:12, 1923.

case of their own) of aneurysms of the hepatic artery and its branches. In 50 instances, the causative factors were known and were, with the number of cases, as follows: general infections, 7; typhoid fever, 2; pneumonia, 5; empyema, 1; osteomyelitis, 3; arteriosclerosis, 12; cholelithiasis, 5; syphilis, 7, and trauma, 8. They did not mention periarteritis nodosa as a factor, as in the cases of Klotz and Walter.

Additional cases of aneurysm of the hepatic artery have been reported by Thompson [6] (erosion of the vessel by a tuberculous gland), Muller [7] and Aschner [8] (atherosclerosis) and Stokes [9] (suspected mycotic aneurysm in a case of malignant endocarditis; see also Eichelter and Knoflach [10]).

The case reported in this paper is that of an aneurysm of the cystic artery, found in association with an ulcerative cholecystitis and cholelithiasis. Because the entire cystic artery was the seat of an inflammatory and toxic process, various stages in the development of the aneurysm could be studied. Its pathogenesis differed from that of any of the aforementioned cases.

For this study, serial sections were made of the cystic artery. Hemalum and eosin, van Gieson and elastica stains were made on alternate sections.

REPORT OF CASE

History.—A white man, aged 58, a machinist, was a habitual drunkard, and had entered the hospital on several occasions after an alcoholic debauch. His history was therefore unreliable. In April 1928, he entered the hospital with impending delirium tremens. On physical examination he was found to be icteric. The heart and lungs were essentially normal. The abdomen was protuberant, and the skin contained many striae albicantes. The liver was 8 cm. below the right costal margin and had a sharp edge. The spleen was also palpable and extended to the crest of the ileum. The rectal examination revealed hemorrhoidal tags. There was a slight edema of the lower extremities. The diagnosis made at the time was that of alcoholic cirrhosis. He remained in the hospital for six days, his jaundice clearing rapidly, and at no time did he complain of abdominal pain.

In October, 1929 (one and one-half years later), he returned to the hospital complaining of a tired feeling and of weakness and cramps in his muscles and legs. He also complained of "spells" characterized by marked weakness and throbbing temporal headache associated with tinnitus and a tendency to see double. On being questioned, he denied having any abdominal distress.

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6. Thompson, W. P.: Tuberculous Aneurysm of the Hepatic Artery, Bull. Johns Hopkins Hosp. **42**:113, 1928.

7. Muller, H. R.: Aneurysm of the Hepatic and Gastroduodenal Arteries with Rupture into the Duodenum, Proc. New York Path. Soc. **20**:46, 1920.

8. Aschner, P. W.: Aneurysm of the Hepatic Artery, Internat. Clin. **2**:334, 1923.

9. Stokes, E. H.: Aneurysm of Hepatic Artery Associated with Acute Endocarditis, M. J. Australia **2**:346, 1926.

10. Eichelter, G., and Knoflach, J. G.: Rupturiertes mykotisches Aneurysma der Arteria gastroepiploica dextra, Deutsches Arch. f. Chir. **198**:416, 1926.

He had had, in the past, influenza, erysipelas and gonorrhea. He said that he had never had a chancre.

Physical Examination.—On physical examination, he was slightly icteric, but not acutely ill. His temperature was normal; the pulse rate was 78, and the respiratory rate, 24 per minute. The blood pressure was 140 systolic and 80 diastolic. The heart and lungs were essentially normal. The liver was 7 cm. below the right, and the spleen, 6 cm. below the left, costal margin. There was no tenderness over the abdomen. The extremities were slightly edematous.

The urine was positive for bile, but was otherwise normal. The stools were light gray and contained no bile.

The results of examination of the blood were: hemoglobin, 75 per cent; red blood corpuscles 3,920,000; white blood corpuscles, 4,850 per cubic millimeter, with 84 per cent polymorphonuclear leukocytes, 12 per cent lymphocytes and 4 per cent eosinophils. The Kahn reaction was negative, and chemical examination of the blood showed that it was normal.

In view of the anemia and the enlarged liver and spleen, the diagnosis was: Banti's disease with cirrhosis of the liver.

Course.—The patient was fairly comfortable until twenty-five days after his admission to the hospital. Then chills and fever suddenly developed (temperature of 103.4 F., taken rectally), and the patient complained of cramplike pains in the abdomen. These symptoms lasted for only a few hours, but the temperature remained slightly elevated for four days, varying from 99 to 100 F.

The stools at the time of the attack and until the time of death were tarry.

After remaining free from fever for six days, the patient again suffered a chill and complained of severe abdominal pain, which was relieved only by a hypodermic injection of morphine sulphate. Five hours later, the pain returned; this time he vomited a large amount of dark, liquid blood and undigested food. His pulse became rapid (120 per minute) and weak; his respirations were labored (36 per minute), and his temperature was subnormal (96.4 F., taken rectally). Eight hours later, he became stuporous. Death occurred twelve hours after the onset of the acute symptoms.

Diagnosis.—The final diagnosis was: Banti's disease with cirrhosis of the liver, acute cholecystitis and cholelithiasis and rupture of an esophageal varix.

Postmortem Examination (Dr. R. H. Jaffé).—The body weighed 175 pounds (79.4 Kg.) and measured 170 cm. in length.

Externally, the skin was of a dirty yellow color; the sclerae were yellow. The mucous membranes were pale. The abdomen was below the level of the chest, but there were striae on the abdomen. The ankles were edematous.

The midline fat of the abdomen was 2 cm. thick. There was about 300 cc. of a dark red fluid in the abdominal cavity. The edge of the liver was at the xiphoid process and at the eighth rib in the right midclavicular line. The transverse colon was firmly adherent to the inferior aspect of the liver. The intestinal loops were moderately distended and covered by thin, blood-tinged fluid. The spleen extended 10 cm. below the left costal arch in the midaxillary line.

The heart weighed 465 Gm. The epicardium was studded with red areas ranging in size from that of a pinpoint to that of a pinhead. The myocardium varied in color from yellowish gray to brown and was very friable.

The gallbladder was distended, measuring 9 by 4.5 by 4 cm. The wall was thickened to a breadth of 6 mm., and was firm and grayish white, and embedded in the liver substance. The cavity was filled by soft, semiliquid, purplish-red masses and many dark-brown concretions, which were from 3 to 5 mm. in diame-

ter. The internal lining of the gallbladder was yellowish white, with irregular defects from 5 to 15 mm. in diameter. These defects had shaggy, overhanging edges and a dark-purplish-gray floor. In the middle of the upper wall was a pea-sized sac that bulged into the cavity and contained an irregular rent, 6 by 5 mm. The sac communicated with a medium-sized artery. In the upper and posterior portion of the wall of the gallbladder was a deep ulcerated area, which surrounded an opening 2 mm. in diameter, that led into the abdominal cavity. The abdominal opening was posterior to the transverse colon. The extrahepatic bile ducts were patent and contained several mulberry-shaped concretions, from

Fig. 1.—Chronic ulcerative cholecystitis, with rupture of an ulcer into the abdominal cavity as designated by the arrow. The wall of the gallbladder is markedly thickened and is embedded in the liver. The duodenum and ascending colon are adherent to the wall of the gallbladder by dense fibrous tissue. The ruptured aneurysm is seen within the gallbladder (about one-third natural size).

3 to 5 mm. in diameter, which were most numerous in the common duct, 2 cm. above the papilla of Vater.

The liver measured 32 cm. transversely, 20 cm. vertically and 10 cm. antero-posteriorly. The surface of the liver was studded with granulations, from 1 to 2 mm. in diameter, which were light yellowish gray and separated by grayish-white lines. The liver was firm in consistency. The cut surface presented granulations like those described.

The esophageal and the superior hemorrhoidal veins were distended and tortuous.

The spleen weighed 2,045 Gm. The surface was smooth and purplish gray, with whitish septal lines. The consistency was soft. The cut surface was purplish red and moderately moist with distinct whitish, slightly elevated follicles, from 1 to 3 mm. in diameter.

The remaining organs presented no significant changes.

Anatomic Diagnosis.—The anatomic diagnosis was: ruptured aneurysm of the cystic artery, with intracystic hemorrhage; chronic ulcerative cholecystitis, with perforation into the abdominal cavity; intra-abdominal hemorrhage; cholelithiasis and multiple stones in the extrahepatic bile ducts; atrophic cirrhosis of the liver; enormous subacute and chronic tumor of the spleen; dilation of the esophageal and upper hemorrhoidal veins; eccentric hypertrophy of the heart and fatty degeneration of the myocardium; severe cloudy swelling of the kidneys; tarry intestinal content, and chronic icterus.

Microscopic Examination.—In the liver, small islands of cells were separated by much fibrous tissue, which was loosely infiltrated by lymphocytes and contained cords of atrophic liver cells and proliferated bile ducts. The liver cells of the islands contained granules of lipoid and of greenish-brown pigment. In the connective tissue septums there were many cells filled with fat and iron pigment.

In the spleen, the reticulum was thickened, and the sinuses, which were wide and filled with blood, stood out distinctly. The pulp contained lymphoid cells, plasma cells and a moderate number of granulocytes. The follicles were small and had no germinal centers; their reticulum was not thickened.

In the gallbladder, the epithelium lining the mucosa was entirely absent. The mucosa was markedly thickened by dense accumulations of plasma cells, lymphocytes, leukocytes and fibroblasts. Newly formed connective tissue and capillaries were abundant. In places, ulcers were noted that at times extended to the muscularis. At one point near the aneurysmal sac, such an ulcerated area extended through the muscularis, to meet a similarly ulcerated area in the serosa, forming a complete rent in the wall of the gallbladder, which was filled with blood. The muscularis was hypertrophic, except in the vicinity of the aneurysm; there the muscle fibers were atrophic, and disappeared entirely at the site of the tear. Extensive hemorrhages, as well as inflammatory cells, were scattered throughout the muscularis and mucosa.

In the main branch of the cystic artery, 2 cm. proximal to the aneurysm, the adventitia was markedly thickened by fibrous tissue. The media was wider than normal as a result of hypertrophy of the muscle fibers and an increase in elastic fibrils. The internal elastic membrane was split. The intima was thickened by an increase of elastic fibrils and connective tissue. The endothelium lining the intima was intact.

From a point 1 cm. proximal to the site of the aneurysm, the artery divided into several branches. These were all affected by one or two processes, degenerative or degenerative and inflammatory.

One of the branches of the vessel was bordered on one side by an accumulation of lymphocytes, leukocytes, plasma cells and histiocytes. The connective tissue in this area was loosened. At this point, the adventitia was markedly thickened by a dense meshwork of fine elastic and connective tissue fibrils. The corresponding media was rarefied and thin, and the nuclei of the muscle fibers were pyknotic or absent. The remaining media was hypertrophied and edematous. The internal elastic membrane was split and presented an increase of elastic fibrils on the

intimal side, so that this portion of the intima was thickened. There were no inflammatory cells in the wall proper.

Continuing distally, the adventitia and media of this branch of the artery were invaded by leukocytes and lymphocytes. The media had a break in its continuity which included the intima. At the site of the tear a thrombus of fibrin and platelets had formed. Serial sections revealed that the vessel was near

Fig. 2.—A branch of the cystic artery, showing hypertrophy of its wall and marked focal perivascular increase of elastic fibrils and fibrous tissue. Elastica stain; × 80.

the inner surface of the gallbladder. There, the adventitia and media were absent, and only the thickened intima remained. However, farther along, this, too, was involved and partly destroyed by the inflammatory process. No outpouching of the intima was evident. The veins and several arteries in the vicinity were occluded by organized thrombi.

The remaining branches of the cystic artery were all the seat of a process different from that described in the foregoing paragraphs. All of these vessels

showed hypertrophy of the media, proliferation of the intima and an increase of fibrous and elastic tissue of the adventitia. This was considered the result of their being embedded in chronically inflamed tissue. In addition to these changes, however, a more recent process was noted, with a definite sequence of events, since many of the vessels were involved in different stages of the disease. A composite of all the changes answers to the following description, according to progression: The media was edematous and at one point became rarefied as a result of a decrease of muscle fibers and a "stretching" of elastic fibrils. In other places, the media had ruptured, and when the rupture included the intima a thrombus of

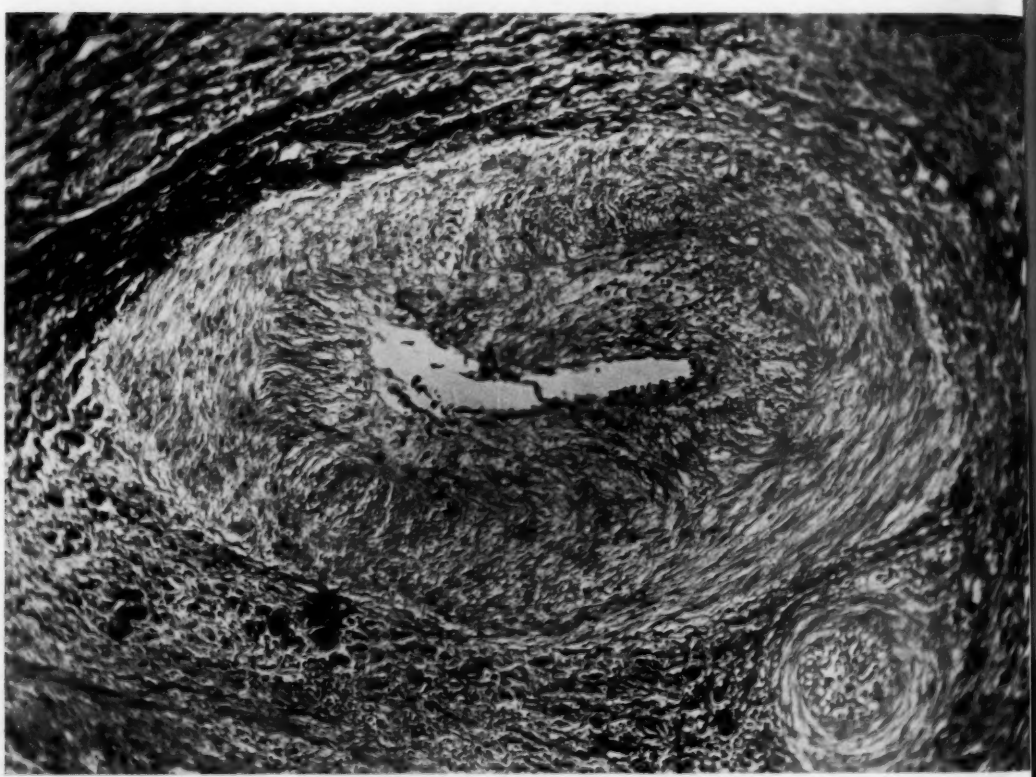

Fig. 3.—A branch of the cystic artery, showing edema and focal rarefaction of media. Note the dense fibrous tissue at the corresponding point in the adventitia. Hemalum and eosin; reduced from × 80.

platelets and leukocytes formed. When the adventitia was also broken, the thrombus, as well as parts of the internal elastic membrane and intima, was found extruded into the perivascular tissue. At times the thrombus became organized, and a spurious aneurysm formed; at other times, small vessels, as they left their site of origin, showed disintegration. Inflammatory cells were absent in the wall or in close proximity about the vessel.

The artery that led to the aneurysm was the seat of a similar process. Here, too, an inflammatory process was lacking.

In the aneurysm, proximally, the intima was markedly thickened, owing to an increase of elastic fibrils and connective tissue and the presence of large branched cells. The lumen was almost occluded as a result of this proliferation. The aneurysmal sac, which was ruptured, was composed of the following layers given in order from the outside inward—a layer of granulation tissue with newly formed capillaries that extended for one-half the distance about the sac and was similar to the granulation tissue of the mucosa of the gallbladder; a thin layer of young connective tissue with fibroblasts, which stained pale reddish pink by van Gieson's method, and which took its origin from the intima; finally, a thick inner coat of

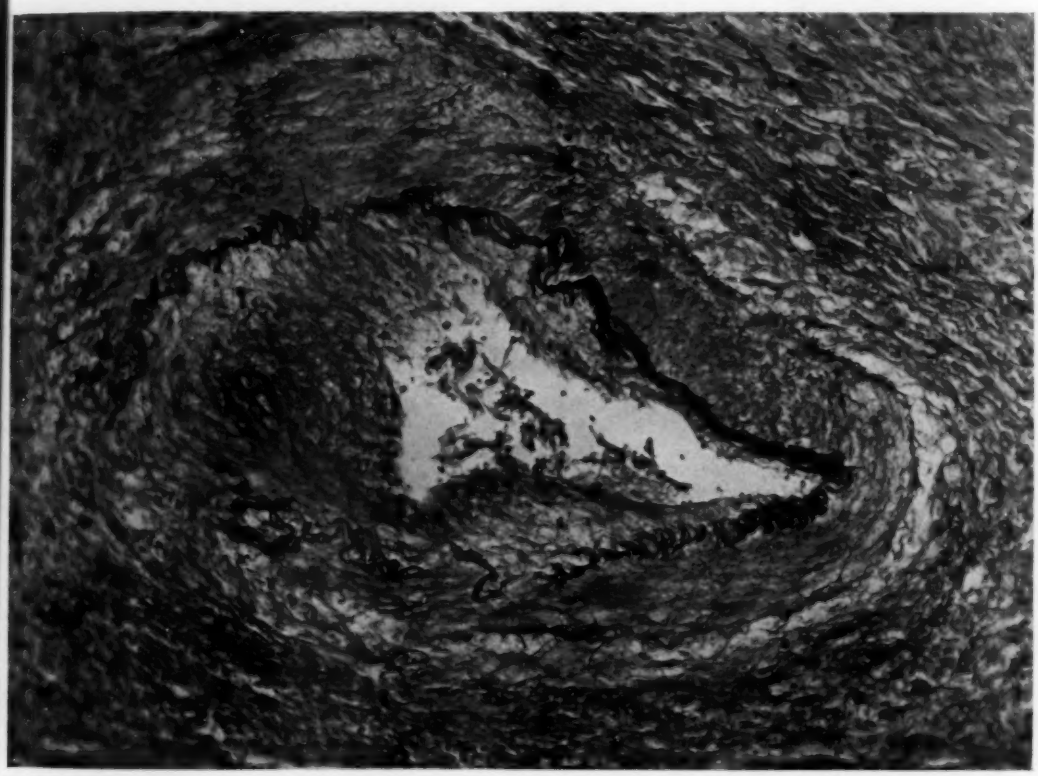

Fig. 4.—An artery showing rupture of its entire wall, with the formation of an organized thrombus at the site of rupture. Note the segmentation of the internal elastic membrane. Elastica stain; reduced from × 80.

laminated layers of fibrin, leukocytes and red cells. The organization became less pronounced as the lumen was approached. The sac was ruptured at the point of its attachment to the wall of the blood vessel.

Several branches of the artery, the site of the origin of which was opposite the aneurysmal sac, showed necrosis, rupture of their walls and formation of thrombi, all as in the process described.

In the cystic artery distal to the aneurysm, both inflammatory and degenerative changes were noted, as described for the portion proximal to the aneurysm.

PATHOGENESIS

The condition responsible for the changes in the cystic artery and the formation of the aneurysm was undoubtedly the inflammatory process in the wall of the gallbladder. This was both acute and chronic. As a result of the chronic process, the blood vessels lying in the wall of the gallbladder showed marked hyperplastic changes in all their coats. Of special interest was the adventitia, which presented an increase not

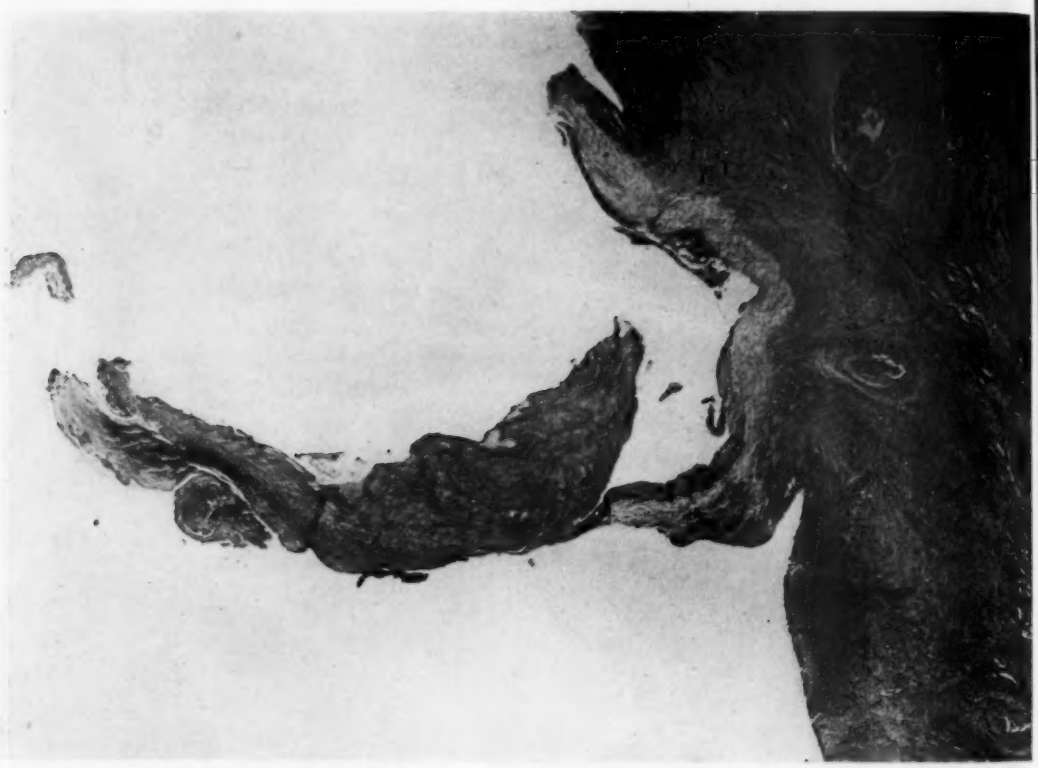

Fig. 5.—Ruptured aneurysm of a branch of the cystic artery. Hematoxylin and eosin; reduced from × 25.

only of fibrous tissue, but also of elastic fibrils. The acute inflammatory process acted directly on the walls of the blood vessels, eroding or obliterating them.

Many of the vessels, however, were the seat of changes not to be accounted for by the inflammatory lesions. These arteries were embedded in fibrous and elastic tissue and were not infiltrated by inflammatory cells. The changes were degenerative, perhaps as a result of the toxic action of the infected bile. The reaction to this toxic substance

was an edema of the muscularis, which was followed by a rarefaction at one point and finally a rupture.

When this tear extended to the intima, a thrombus formed at this site. If the adventitia was also involved, the pressure of the blood forced the thrombus, as well as portions of the intima and internal elastic membrane, into the perivascular tissue.

If the artery was of medium caliber and the process a gradual one, the thrombus at the site of rupture became organized and formed the wall of a spurious aneurysm.

The latter was the mechanism of the formation of the large aneurysm. It was, however, of some duration, for the aneurysm communicated with the lumen of the vessel and can thus be classified as a true aneurysm (Kaufmann,[11] Menetrier[12]).

Because the rupture of the aneurysm occurred at its attachment to the arterial wall, it is deducted that the blood pressure within was responsible, rather than a passing stone, as in such a case the most exposed part would have been the site of rupture.

DIFFERENTIATION FROM PERIARTERITIS NODOSA

The resemblance of some of the lesions of the vessels described to periarteritis nodosa warrants a differential diagnosis.

Grossly, the gallbladder in periarteritis nodosa is fairly typical. The mucosa is edematous, discolored a dark brown and at times may be studded with hemorrhagic infarcts. On palpation along the cystic artery spindle-shaped nodules are felt, like a string of pearls (Klotz,[2] Walter,[4] Gruber,[13] Wesemann,[14] Singer[15]). Rarely, is the gallbladder the seat of a pyemic process (Walter, Gruber).

In the case reported, none of these characteristics was found, but instead an acute exacerbation of a chronic cholecystitis and cholelithiasis.

Microscopically, the end-stages of both conditions are similar in that there is occlusion of the vessels by thrombi with organization and formation of aneurysm. The earlier stages, however, differ appreciably. The process, in both instances begins in the media. In periarteritis nodosa, there are edema, fibrinous exudate, hyalinization and necrosis of the media. A moderate to extensive infiltration by leukocytes (especially

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12. Menetrier, M.: Des Aneurysms, Arch. de méd. exper. **2**:97, 1890.

13. Gruber, G. B.: Zur pathologische Anatomie der Periarteritis nodosa, Virchows Arch. f. path. Anat. **245**:123, 1923.

14. Wesemann: Ein Fall von Arteritis nodosa, Inaug. Diss., Köln, 1921.

15. Singer, H. A.: Periarteritis Nodosa, Arch. Int. Med. **39**:865, 1927.

eosinophils) lymphocytes and plasma cells follows (Gruber,[13] Arkin [16]). Later, the process extends to involve the adventitia and intima. Thrombi and formation of aneurysms are common.

In the case reported, the media was edematous and underwent degenerative and atrophic changes rather than necrotic and inflammatory ones. There was no cellular exudate in the wall of the vessel. (This refers to the vessel in which the aneurysm formed).

Finally, in periarteritis nodosa, the vessels of more than one organ are involved (Kussmaul and Maier,[17] Gruber,[13] Klotz,[2] Walter,[4] Lemke,[18] Wesemann,[14] Singer [15]), although localized cases have been described (Keegan [19]).

In the reported case, only the cystic artery was involved.

COMMENT

In aneurysms of the hepatic artery and its branches, rupture and exsanguination is a common cause of death (Schmidt [20]). In about 70 per cent of the cases reported in the literature the patient died in this manner. Rupture into the peritoneal cavity is most common. In the two cases of ruptured aneurysm of the cystic artery, rupture was into the gallbladder or into its duct.

In the case reported in this paper, the aneurysm ruptured into the gallbladder and produced enough intracystic pressure to rupture an ulcer of the wall of the gallbladder. Thus an intraperitoneal hemorrhage resulted.

The association of aneurysm of the cystic artery with atrophic cirrhosis of the liver has not been heretofore reported. Three cases of the latter have occurred, however, with aneurysms of the hepatic artery (Ledieu,[21] Sacquépée,[22] Wältzold [23]). The etiology given for two of these cases involved syphilitic endarteritis. In the third case the etiology was not given.

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16. Arkin, A.: Periarteritis Nodosa, Am. J. Path. **6**:401, 1930.

17. Kussmaul, A., and Maier, R.: Ueber eine bisher nicht beschriebene eigenthümliche Arterienerkrankung, die mit Morbus Brightii und rapid fortschreitender allgemeiner Muskellähmung einhergeht, Deutsches Arch. f. klin. Med. **1**:484, 1866.

18. Lemke, R.: Ein weiterer Beitrag zur Frage der Periarteritis nodosa, Virchows Arch. f. path. Anat. **245**:322, 1923.

18. Lemke, R.: Ein weiterer Beitrag zur Frage der Periarteritis nodosa, Arch. Int. Med. **36**:189, 1925.

20. Schmidt, M. B.: Tödliche Blutung aus einem Aneurysma der Leberarterie bei Gallensteinen, Deutsches Arch. f. klin. Med. **52**:536, 1894.

21. Ledieu: Des Aneurysms, J. de méd. de Bordeaux, 1856, p. 125.

22. Sacquépée, B.: Blutung im Inneren der Leber mit Durchbruch in die Bauchhöhle, Zentralbl. f. path. Anat. **11**:748, 1900.

23. Wältzold, D.: Leberruptur mit tödlicher Blutung infolge Berstens eines oberflächlichen Aneurysmas, Münch. med. Wchnschr. **53**:2107, 1906.

It is possible that the same inflammatory processes, specific or non-specific, are responsible for the formation of the aneurysm, as well as for the cirrhosis of the liver.

CONCLUSIONS

A case of aneurysm of a branch of the cystic artery is reported, which had ruptured into the gallbladder and, in turn, into the abdominal cavity, as a result of ulcerative cholecystitis and cholelithiasis.

A toxic, degenerative process of the cystic artery is described as the pathogenesis of the aneurysm. This process consists of an edema of the media, followed by rarefaction and rupture at one point. When the tear extends to the intima, a thrombus forms, which, if the process is slow, becomes organized and forms the wall of an aneurysm. When circulation is established through the aneurysm, the possibility of rupture is great.

THE HISTOLOGY OF EXPERIMENTAL TUBERCULOSIS IN DIFFERENT SPECIES

A COMPARATIVE STUDY *

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By the intracerebral method of inoculation described in a previous paper,[1] it is possible to obtain well defined lesions of tuberculosis in the tissues of many animals that are highly resistant to the infection by the ordinary means of exposure. For example, it is practically impossible to induce demonstrable lesions of the disease in chickens by the intravenous or subcutaneous injection of the human or bovine forms of the organism, yet when these forms are injected into the substance of the brain pronounced lesions result in this organ. The guinea-pig, which is very susceptible to infection with the tubercle bacillus of either human or bovine origin by the usual methods of exposure, is extremely resistant to the avian form of the organism. When the guinea-pig is inoculated intracerebrally with organisms of avian origin, definite lesions of tuberculosis are established. Again, the dog, although susceptible to infection with the human and bovine varieties of the tubercle bacillus, is extremely resistant to organisms of avian source when exposed by intrabronchial, intravenous, subcutaneous or intraperitoneal injections, or by feeding.[2] However, when the bacteria are introduced into the brain through a cranial perforation, definite and extensive tuberculous lesions develop.

As a consequence of the experiments described [1] and of others, I have been able to obtain lesions induced by the three forms of *Mycobacterium tuberculosis* in certain species in which this has heretofore not been possible. The tissues obtained from the respective species have been utilized in a comparative study of the histologic changes to determine whether the character of the host's reaction to the bacillus of tuberculosis is dependent on the form of the organism present (whether human, bovine or avian) or whether the character which the lesions assume is dependent on the species harboring the infection. In other words, does the anatomic nature of tuberculosis in a given

* Submitted for publication, Jan. 6, 1931.

* From the Division of Experimental Surgery and Pathology, the Mayo Foundation.

1. Feldman, W. H.: Am. Rev. Tuberc. **21**:400, 1930.

2. Feldman, W. H.: J. Am. Vet. M. A. **76**:399, 1930.

animal differ with the type of organism responsible for the lesions or are the tuberculous lesions in a given animal similar regardless of the source of the organism?

METHODS

All cultures of *Mycobacterium tuberculosis* used for the production of lesions in this study were original strains isolated from human, bovine and avian tissues. The type of the respective strains was challenged by the inoculation of guinea-pigs, rabbits and chickens before the cultures were accepted as suitable for the experiment. In determining the true type of a given organism by inoculation of an animal the following tests of pathogenicity were carried out: (1) Guinea-pigs were inoculated subcutaneously or intraperitoneally and (2) chickens and rabbits were inoculated intravenously. Animals living at the expiration of ninety days were killed for necropsy. All chickens used were previously tested by tuberculin. The degree of susceptibility, as determined by the presence of demonstrable lesions of tuberculosis, is shown in the tabulation.

When the disease was induced by the intracerebral route of inoculation, the method of exposure was the same for all animals. With the animal under ether anesthesia the injection was effected through a small cranial perforation,

Results of Tests for Pathogenicity of the Three Types of the Tubercle Bacillus Employed in the Experiments

Type of Organism	Degree of Infection in Animal Inoculated		
	Guinea-Pig	Rabbit	Chicken
Human	+++	+	0
Bovine	+++	+++	0
Avian	0	+++	+++

care being taken to minimize the possibility of extraneous contamination. The dosage used varied with the size of the animal, being from 0.1 to 1 cc. of a saline suspension prepared from cultures growing on egg or potato medium. In order to provoke possible lesions most of the suspensions were purposely made rather dense, and an attempt was not made to estimate the number of bacteria present in each cubic centimeter.

Material was selected as soon after death as possible and fixed in 10 per cent neutral formaldehyde solution. After fixation the tissues were embedded in paraffin, and sections were prepared. From each block two series of sections were obtained. One series was stained with hematoxylin and eosin, and the other was treated with carbolfuchsin-hematoxylin by a method previously described.[3] Although a large number of different species of animals were used in a series of experiments pertaining to the pathogenicity of the various bacillary forms of *Mycobacterium tuberculosis,* the observations recorded here were confined to the chicken, the guinea-pig, the rabbit and the dog.

PATHOLOGIC ANATOMY

Chicken.—Material was obtained from chickens that had died or had been killed subsequent to an injection of one of the three types of the tubercle bacillus. With the avian strain a fatal tuberculous infec-

3. Magath, T. B., and Feldman, W. H.: Am. Rev. Tuberc. **22**:514, 1930.

tion was obtained by either the intravenous or the intracerebral method of inoculation, but death resulted much earlier by the latter method than by the former. The duration of the disease varied from 3 to 10 weeks, dependent on the method of inoculation used. Since it was impossible to incite demonstrable lesions in the chicken by either the human or the bovine form of the organism by the intravenous or by the subcutaneous method of exposure, the only lesions obtained from the common fowl which were due to either of these strains were those

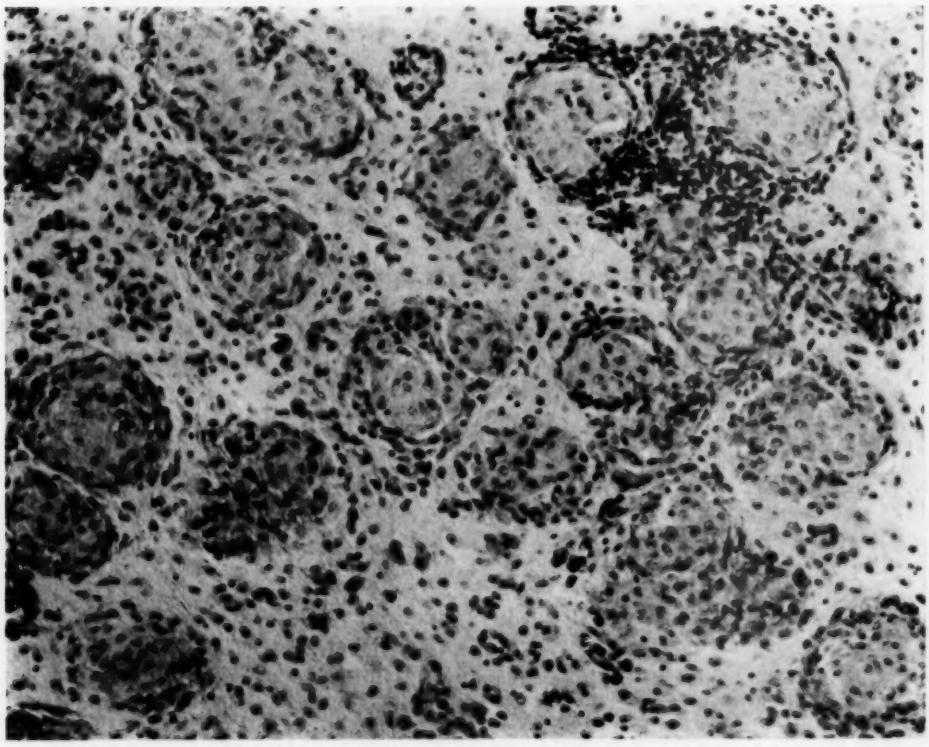

Fig. 1.—Lesions of tuberculosis in the cerebrum of a chicken. Death occurred twenty-eight days after the intracerebral introduction of the avian organism. The multiple follicular arrangement usually assumed by the monocytic cells in the tissues of the chicken following an injection with the organism of tuberculosis is shown; × 200.

that resulted from the intracerebral method of injection. Of the two birds inoculated in this manner with the organism of human source, one died after a period of 56 days, and the other was killed for necropsy 136 days subsequent to the inoculation. The two that were inoculated with the bacteria of bovine origin were killed for necropsy after 119 days.

In the chickens inoculated intracerebrally with the avian form of the organism lesions were found to be distributed throughout the brain, liver and spleen in such a manner as to indicate a generalized infection. With the human and bovine strains, however, demonstrable lesions were confined to the brain.

A study of the histologic reactions induced in the respective chickens by the three different strains of organisms revealed a remarkable similarity which was strikingly consistent throughout the course of the

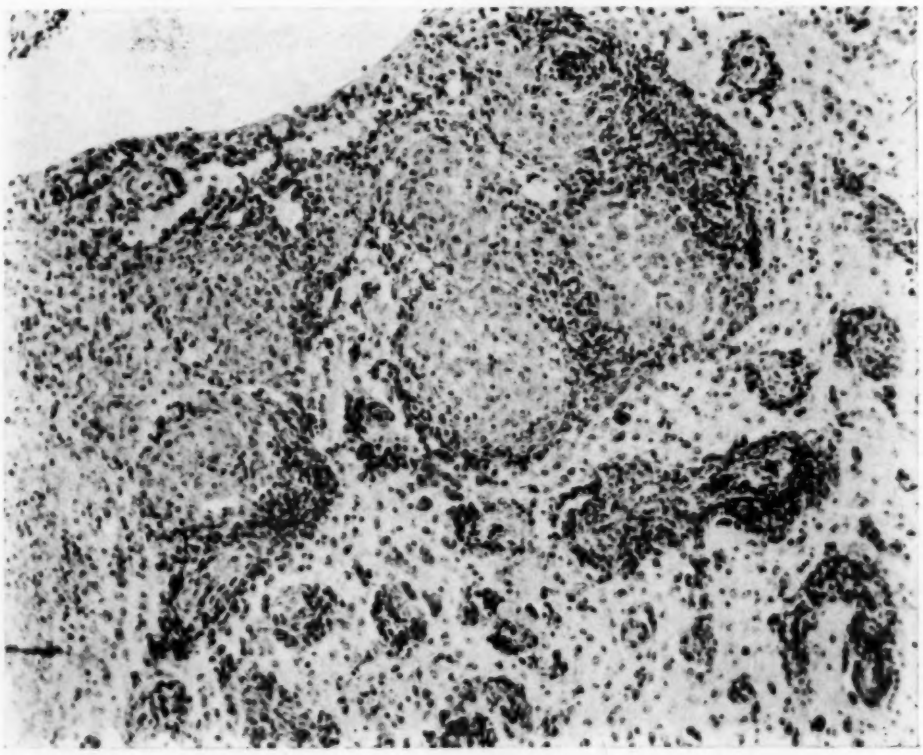

Fig. 2.—The cellular reaction in the cerebrum of a chicken induced by the intracerebral injection of the human tubercle bacillus. The chicken was killed 136 days subsequent to the injection of the infective material. The monocytic cells are arranged in circumbscribed spherical masses significantly like those in figures 1 and 3.

disease. Regardless of the source of the etiologic agent, the initial cellular response was the same. It consisted of multiple, discrete, spherical collections of monocytic cells which exhibited a persistent tendency to retain their focal character, even though the amount of infection present stimulated the formation of large numbers of them in masslike formation (figs. 1, 2 and 3). The lesions were also charac-

terized, particularly in the early stages, by an attempt at encapsulation. The monocytic cell constituting the unit of the respective lesions was of a rather large size and exhibited a marked tendency to assume an epithelioid character.

Necrosis seemed to occur at about the same time regardless of the type of the etiologic organism. It was usually of a coagulative or hyaline character and revealed a tendency gradually to become caseous. Necrosis began in the central portions of the respective lesions and

Fig. 3.—Multiple tuberculous lesions in the cerebrum of a chicken that was killed 119 days subsequent to the intracerebral injection of the bovine organism. The central lesion had become necrotic; × 130.

progressed peripherally. Calcification, although not prominent in any of the material studied, occasionally appeared. In those lesions in which necrosis was evident the monocytic cells in contact with the necrobiotic elements were arranged in palisade formation with the long axis of the cells toward the center of the lesions. The nuclei of these cells were situated in the extreme peripheral portion of the cytoplasm, and the opposite ends of the respective cytoplasmatic processes merged

imperceptibly with the necrotic cellular detritus. Giant cells of the Langhans type were present in some of the older lesions.

Many of the lesions which had been provoked by the human and bovine forms of the tubercle bacillus revealed peripheral lymphocytic response (figs. 2 and 3). This varied in amount from a few cells to a large accumulation, even within the limits of a given section. Variable numbers of acid-fast bacilli were demonstrated within the lesions of all tissues studied. They were most numerous in the earlier lesions and apparently were reduced in number as the duration of the disease was prolonged.

Comment: Tuberculous infection in the tissues of the chicken when induced by any of the three forms of the tubercle bacillus is characterized by the appearance of definitely focal, circumscribed collections of monocytic or epithelioid cells of a rather large, clear type. The lesions, which are often multiple, may become confluent, but even though a conglomerate tubercle results, the identity of the separate follicle-like masses of epithelioid cells is usually maintained and is discernible.

Guinea-Pig.—It was not possible to provoke demonstrable tuberculosis in the guinea-pig with the organism of avian origin by either the subcutaneous or the intraperitoneal route of inoculation. Lesions, however, were obtained when the bacteria were deposited within the substance of the brain. By the intracerebral method of exposure a tuberculous infection was established which proved fatal in from eighteen to fifty-seven days, with discernible signs of the disease in the brain, liver and spleen and occasionally involvement of the lung. With the human and bovine forms of the bacillus lesions were readily produced by injecting the organisms either subcutaneously or intraperitoneally, death occurring as early as twenty-three days afterward. Animals living at the expiration of eight weeks were killed for necropsy. By the procedure described it was possible to secure with each of the three forms of the bacillus definitely recognizable lesions of comparable duration for the purpose of a comparative study.

The changes established by the respective bacterial strains were practically the same throughout the various animals used in this phase of the study. They differed materially, however, from those induced in the chicken. Instead of the monocytic cells exhibiting a discrete focal arrangement as in the common fowl, they assumed an entirely different deposition in the guinea-pig. They appeared in the earlier stages in such organs as the liver and the brain as compact, diffuse accumulations with very irregular outlines (figs. 4, 5 and 6). In the spleen the lesions in every instance had their inception in the malpighian body, where they expanded peripherally without demonstrable evidence

of encapsulation. The appearance of giant cells of the Langhans type was so inconsistent in the guinea-pig material studied as to make it difficult to interpret the rôle of this cell in the tuberculous reaction. It appeared in some of the lesions of animals that died as early as twenty days after inoculation, although in others in which the lesions were of comparable duration it was not seen. Again it was occasionally present in lesions of from six to eight weeks' duration. A remarkable exhibition of these cells appeared in the liver, spleen and renal lymph

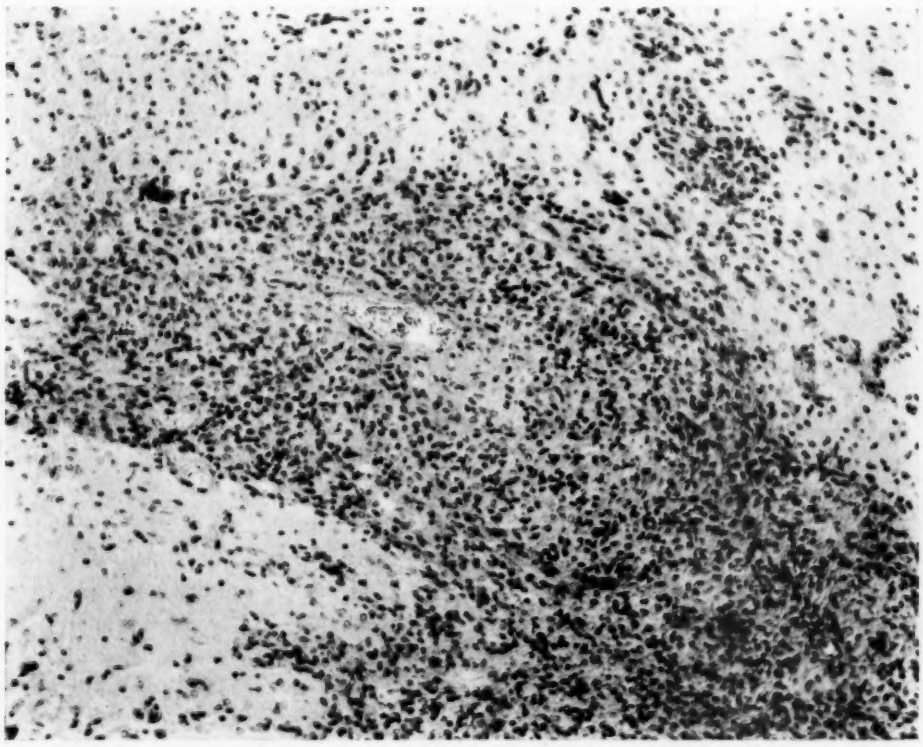

Fig. 4.—Cellular reaction (× 150) in the brain of a guinea-pig that died twenty days subsequent to an intracerebral injection of the avian organism. The monocytic cells are disposed in a diffuse manner. This figure may be contrasted with figure 1.

node of a guinea-pig that died fifty-seven days after intracerebral injection of organisms of avian origin. The interior of each cell unit was filled to capacity with acid-fast bacilli.

As the lesions expanded the central portions of many eventually became necrotic. The necrosis was usually of a caseous nature, although that of coagulative type was occasionally seen. Not infrequently both types were discernible within a single microscopic field. Calcification

was not observed in any of the lesions examined. Acid-fast organisms were demonstrated within the lesions of all tissues studied.

Comment.—In the guinea-pig the three types of tubercle bacillus produced lesions which were practically identical in their morphologic aspects. The lesions were characterized in their earlier stages by closely arranged, diffuse masses of monocytic cells, disposed in an irregular, nonconventional manner, and in this regard they differed materially from the lesions produced by the same organisms in the chicken. Fibrosis

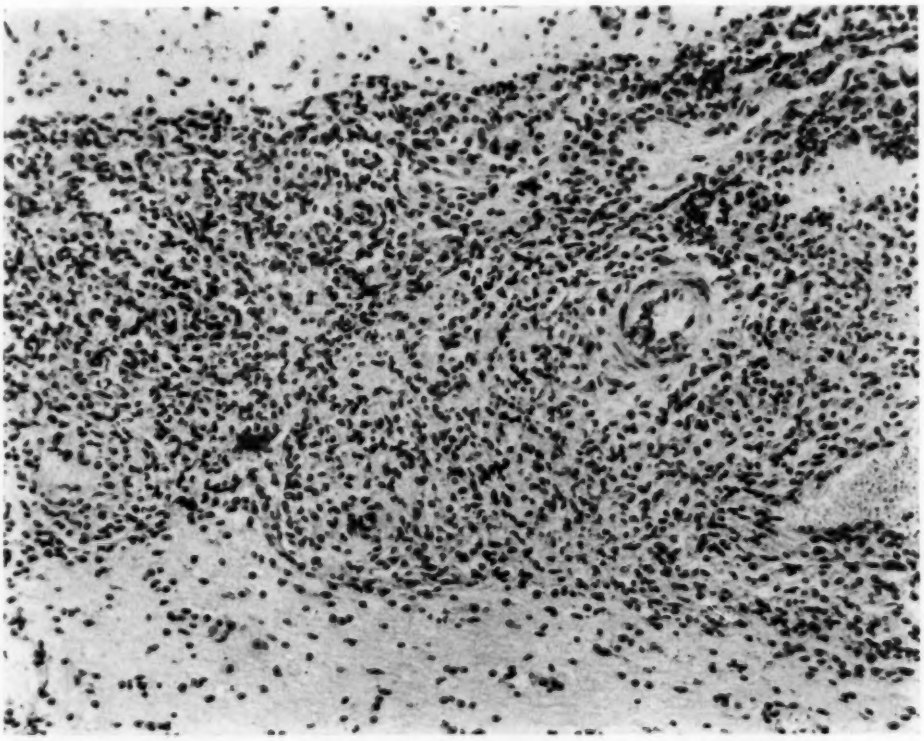

Fig. 5.—Tuberculous lesion (× 150) in the brain of a guinea-pig that died twenty-three days after an intracerebral inoculation of the human organism. There is no tendency toward tubercle formation such as occurred in the brain of the chicken, shown in figure 2.

or attempted encapsulation was not observed. Necrosis without calcification finally changed the character of many of the separate cellular accumulations, although the peculiar palisade arrangement of the cells adjacent to the necrotic tissue, which was so evident in the lesions of the chicken, was not seen in the lesions of the guinea-pig.

Rabbit.—A tuberculous infection was established in rabbits by the intravenous injection of bacteria representing each of the three different forms of tubercle bacillus. The disease was also produced by the

introduction of each of the three bacillary forms into the substance of the cerebrum, and in one instance it was produced by subcutaneous inoculation of the bovine form of the organism. The duration of the lesions in the respective rabbits varied from 11 to 250 days. The earlier lesions were obtained following intracerebral inoculation, whereas the animals in which lesions were obtained after 250 days were those inoculated intravenously with organisms of human origin and finally killed for necropsy.

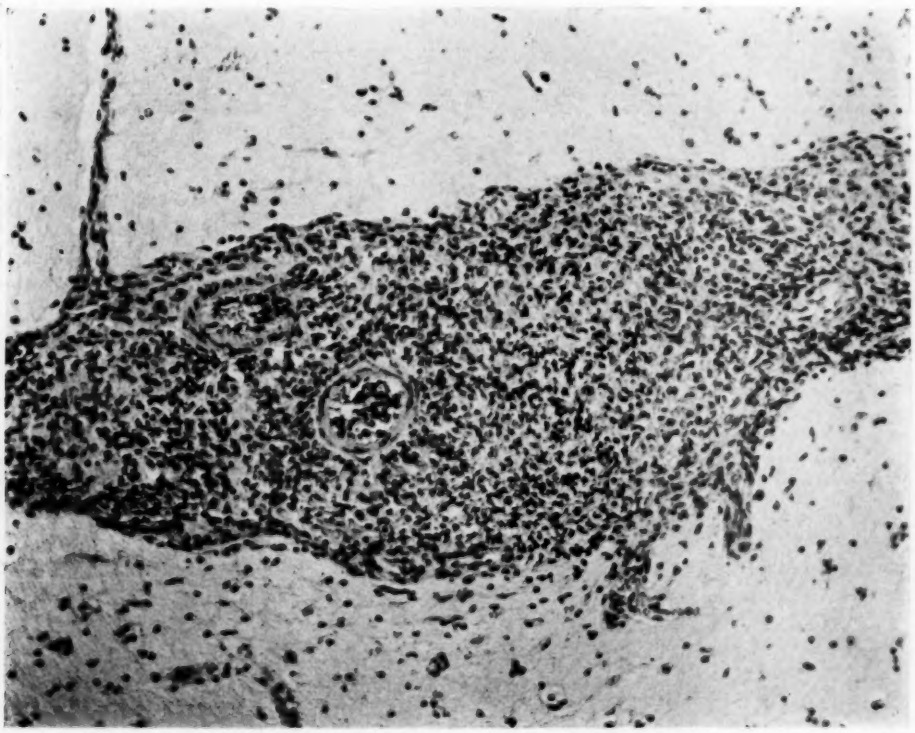

Fig. 6.—Lesion of tuberculosis (× 150) in the brain of a guinea-pig that died twenty days following the intracerebral injection of the bovine organism. The histologic appearance of the cellular reaction is not essentially different from that observed in figures 4 and 5.

Comparison of the individual lesions of comparable duration in the various rabbits showed that there were no essential differences in the character of the histologic reaction to the three forms of the infecting agent (figs. 7, 8 and 9). There were, of course, notable differences in the degree or in the extent of the infection due to variations in the inherent susceptibility of the rabbit to the three bacillary forms of the organism. The rabbit is exceedingly vulnerable to organisms of

bovine and avian origin and considerably less so to organisms obtained from human beings. As a consequence one observes differences in the cellular reaction which are indicative of the degree to which the respective organisms are able to express the full measure of their pathogenicity.

In general, however, the lesions were made up of irregular accumulations of monocytic or epithelioid cells, many of which, with the exception of the lesions of the lung, exhibited a marked tendency to undergo early central necrosis. The Langhans type of giant cell was

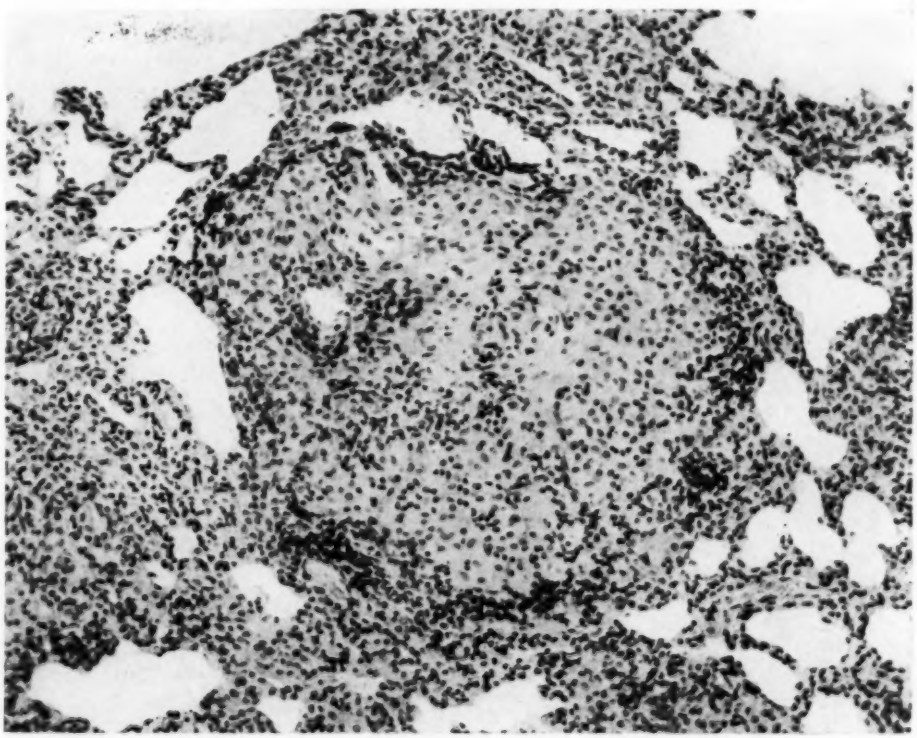

Fig. 7.—Tuberculous lesion (× 150) in the lung of a rabbit that died ninety-eight days after receiving an intravenous injection of bacilli of avian tuberculosis.

frequently present in most of the tissues studied, and many of the lesions of long duration possessed variable amounts of mineral salts. When the disease was rapidly progressive or of long standing, many of the individual cellular units or tubercles showed a tendency to coalesce. In the lungs of those animals in which the disease had continued for a protracted period the formation of abscess with occasional cavitation was observed.

Although there were minor differences in the appearance of some of the lesions in the respective animals, the differences were due to the

different anatomic situations in which the lesions appeared rather than to a specific cellular response to the presence of a particular form of *Mycobacterium tuberculosis*. The splenic lesions were confined rather consistently in the early stages to the malpighian bodies, whereas those in the lung, liver and kidney were not restricted by definite anatomic limitations. Many of the lesions of prolonged duration stimulated the production of large numbers of lymphocytic cells, which were present in the zone immediately adjacent to the uninvolved tissues. Connective

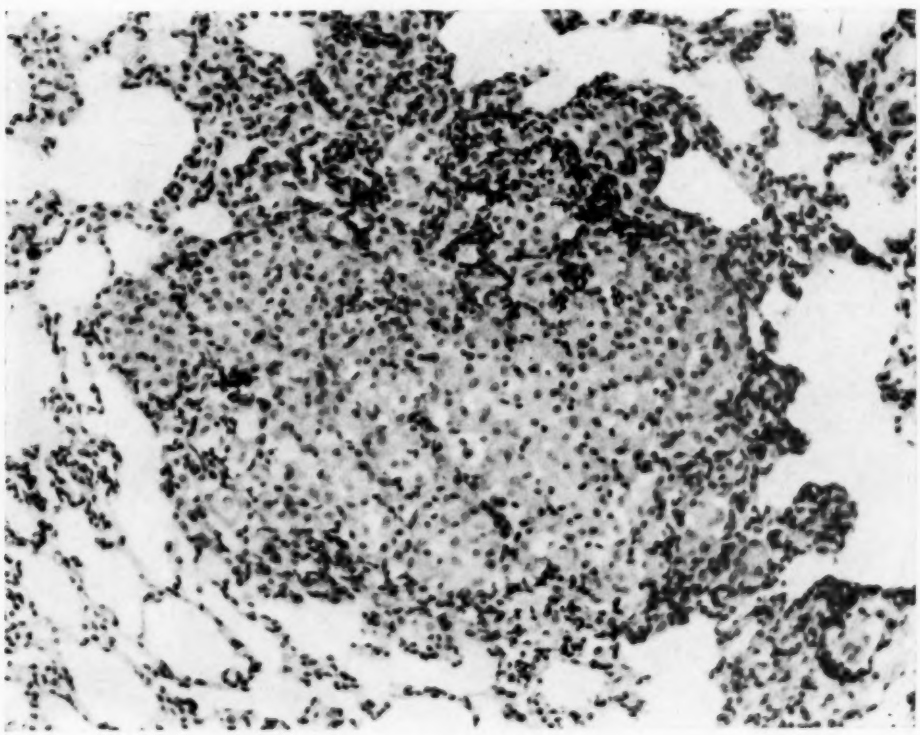

Fig. 8.—A focal accumulation of epithelioid cells (× 180) in the lung of a rabbit that was killed 250 days subsequent to an intravenous injection of the human tubercle bacillus.

tissue encapsulation or fibrosis was not associated with the lesions in the tissues examined. The cerebral lesions were practically identical, regardless of the source of the infecting organism. They were rather widespread and usually caused the death of the animal within a relatively short time, from eleven days to three weeks. In tissues which were appropriately stained, acid-fast organisms were demonstrated in all lesions studied.

Comment: The lesions of tuberculosis in a series of rabbits following the experimental production of the disease with the three different

forms of the infecting organism were without significant differences (figs. 7, 8 and 9). They were characterized by the formation of irregular masses of monocytic or epithelioid cells, and the central portion of many became caseated within a relatively short time. Giant cells were numerous, and encapsulation was not apparent.

Dog.—Lesions of tuberculosis were provoked in dogs by each of the three bacillary forms of the organism when the infective agent was introduced intracerebrally. As previously reported,[2] dogs proved

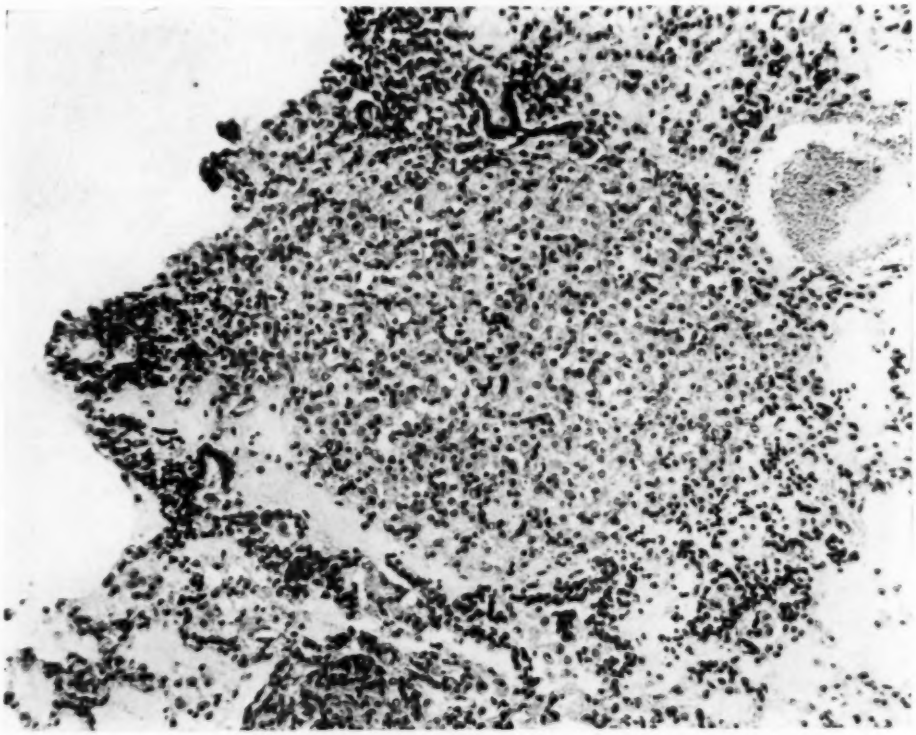

Fig. 9.—Tuberculous lesion (× 150) in the lung of a rabbit. Death occurred 154 days after a subcutaneous inoculation of bacilli of bovine tuberculosis.

exceedingly resistant to the avian form of the bacillus by every route of exposure except by way of the brain. Infection established in this way with organisms isolated from a chicken, produced lesions in the brain, spinal cord, liver and occasionally in the spleen; the lungs escaped demonstrable involvement in every instance. The human and bovine forms of the tubercle bacillus, when injected intracerebrally, set up lesions in the lungs, besides those in the liver, brain and spleen. Lesions were also obtained in the lungs and livers of dogs that were inoculated intravenously with bacilli of bovine and human origin.

In dogs, as in the other species used, a fatal tuberculous infection resulted much earlier following the intracerebral introduction of the infection than by the other means used to establish the disease. Those inoculated intracerebrally succumbed in from eighteen to sixty-three days, and those inoculated intravenously survived for a period of seventy-three days or until they were killed for necropsy after one year.

Since the brain and the liver were the only organs to be consistently affected by each of the three forms of the infecting organisms, the comparative study of the resultant lesions was limited to tissues obtained from these organs. A detailed account of the pathologic changes following the exposure of dogs to bacilli of avian tuberculosis has been recorded elsewhere.[4]

When dogs were inoculated with organisms of avian origin the lesions were perhaps somewhat more extensive, and the cerebral tissue was more involved, than when lesions were produced by either the human or bovine forms of the bacillus. With this exception the character of the cellular reaction was essentially the same regardless of the origin of the etiologic bacteria. Even the lapse of time did not materially alter the histologic picture in the respective animals. It persisted as a more or less irregularly diffuse collection of closely packed monocytic cells without evident encapsulation, but with an occasional appearance of lymphocytic infiltration of the peripheral portion of the lesion. The monocytic cells did not assume an "epithelioid" appearance. The lesions were situated either just under the pia mater, which they frequently followed into the depths of the sulci, or within the substance of the cerebral tissue. In many of the brains, lesions were present in both situations, and the lesions often appeared to have had a perivascular inception. The formation of concentric, tubercle-like structures or giant cells was not observed. Necrosis of the central portion of some of the lesions induced by the avian organism was observed, and the same retrogression was present to less degree in a few of the lesions that developed as a consequence of the human organism. Calcification was not observed in any of the lesions examined. Acid-fast organisms were present within the lesions of all tissues studied, and from those in which cultures were attempted organisms possessing the usual characteristics of *Mycobacterium tuberculosis* were obtained.

A study of the sections prepared from the livers of dogs that died as a consequence of the intracerebral inoculation of each of the three forms of the tubercle bacillus revealed lesions in which there was no marked dissimilarity. The majority of the lesions, regardless of their

4. Feldman, W. H.: Am. J. Path. **7**:147, 1931.

duration, appeared as ovoid or irregularly spherical masses of monocytic cells of the same character as those which constituted the lesions in the cerebrum. The lesions, which were numerous, were situated rather promiscuously throughout the liver. In none of them could the formation of a capsular structure be discerned, and giant cells of the Langhans type were absent. Necrosis or calcification was not observed. Acid-fast organisms, although demonstrable, were not numerous, except in one liver in which the lesions had been induced by the intravenous

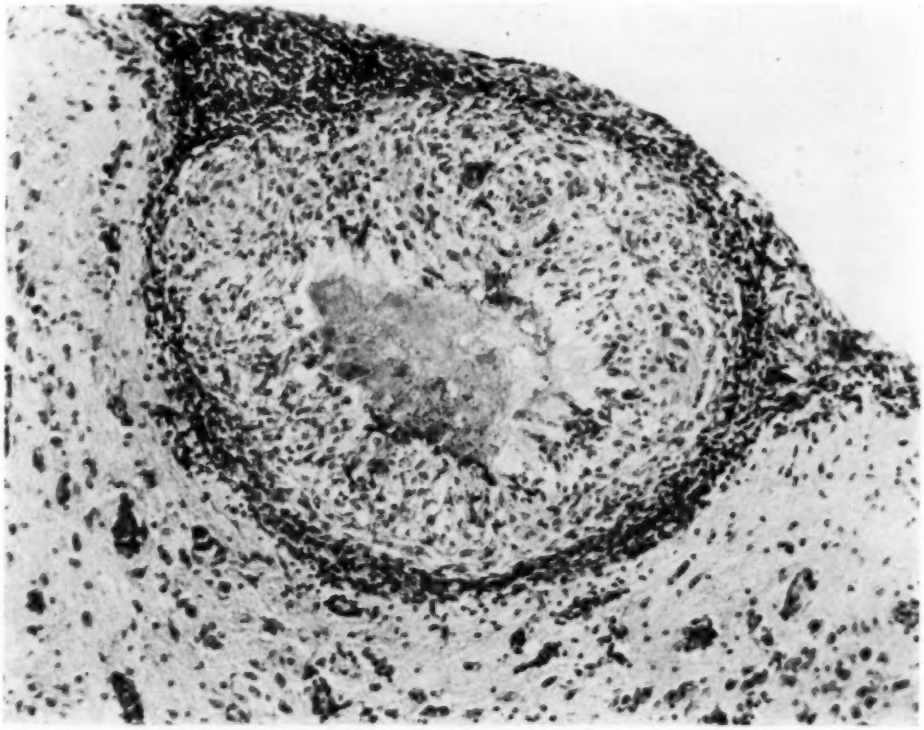

Fig. 10.—Tubercle (× 200) in the liver of a chicken in a case of spontaneous tuberculous infection. The lesion, which is undergoing necrosis, is definitely circumscribed. This figure may be compared with figure 11.

injection of the human form of the organism. The lesions in this instance differed somewhat from the ones I have described in that they were much more extensive. They likewise exhibited less tendency to produce the focal type of cellular formation. Instead, the reaction was diffuse and showed a predilection for the perilobular portions of the organ. In this material an occasional cell form suggestive of the Langhans type of giant cell could be seen, and tremendous numbers of acid-fast bacilli were present.

Comment: Lesions produced experimentally in the brains and livers of dogs by each of the three types of the tubercle bacillus were found to be alike, except for a few minor differences which were due, perhaps, to certain anatomic peculiarities of the involved organs. The lesions were characterized by the presence of monocytic cells arranged in compact masses without evident encapsulation or typical tubercle formation. The lesions, which were rather extensive and numerous, showed only a slight tendency toward retrogression.

Several tuberculous livers of swine, obtained from abattoirs, also were studied. The lesions were of a multiple, miliary character, and emulsions prepared from the diseased tissue and injected into chickens tested with tuberculin eventually produced extensive lesions of typical avian tuberculosis. Cultures obtained from portions of the original emulsions resembled the avian form of the organism in every way. A comparison of the lesions that occurred in the livers of swine with those which resulted in the livers of the inoculated chickens showed great dissimilarity. As has been mentioned, the lesions in the chicken were like those which are usually seen following a spontaneous tuberculous infection in this animal (fig. 10). The lesions were focal and more or less discrete, with a rather definitely circumscribed, irregularly spherical contour. The lesions in the livers of swine, however, were irregularly diffuse, consistently larger than the lesions of the fowl, and with no discernible effort on the part of the connective tissue elements to establish a zone of demarcation between the cells of the lesions and uninvolved hepatic tissue.

COMMENT

Although these studies have made it possible to observe the reaction of several different species of animals to each of the three varieties of the bacillus of tuberculosis, no claim is made that similar lesions would be found if the disease could be studied following its spontaneous inception in the respective species. The usual chronicity of the infection following its spontaneous induction gives the host an opportunity for a much fuller expression of the protective mechanism than is usually possible following the experimental production of the disease. However, lesions that had existed from three months to one year were sufficiently established in their histologic design to enable one to foresee with some degree of accuracy what the ultimate anatomic reaction was to be. Also it seems logical to assume that significant morphologic differences should become evident rather early in the pathogenesis of the respective lesions, particularly if one considers the nature of the development of the tuberculous process in the common fowl. Although the tubercle is rightly considered the anatomic unit of tuberculous infection, in the chicken it is subject to some histologic variation

as compared with the lesion in the lower mammals. This became apparent from the fact that each of the three forms of *Mycobacterium tuberculosis* induced lesions in the brains of chickens which were essentially identical, whereas the same bacteria produced in other species, including the rabbit, guinea-pig and dog, lesions which were unlike those produced in chickens.

In general it might be said that the lesions of tuberculosis in the chicken differed from those in mammals by the monocytic cells early

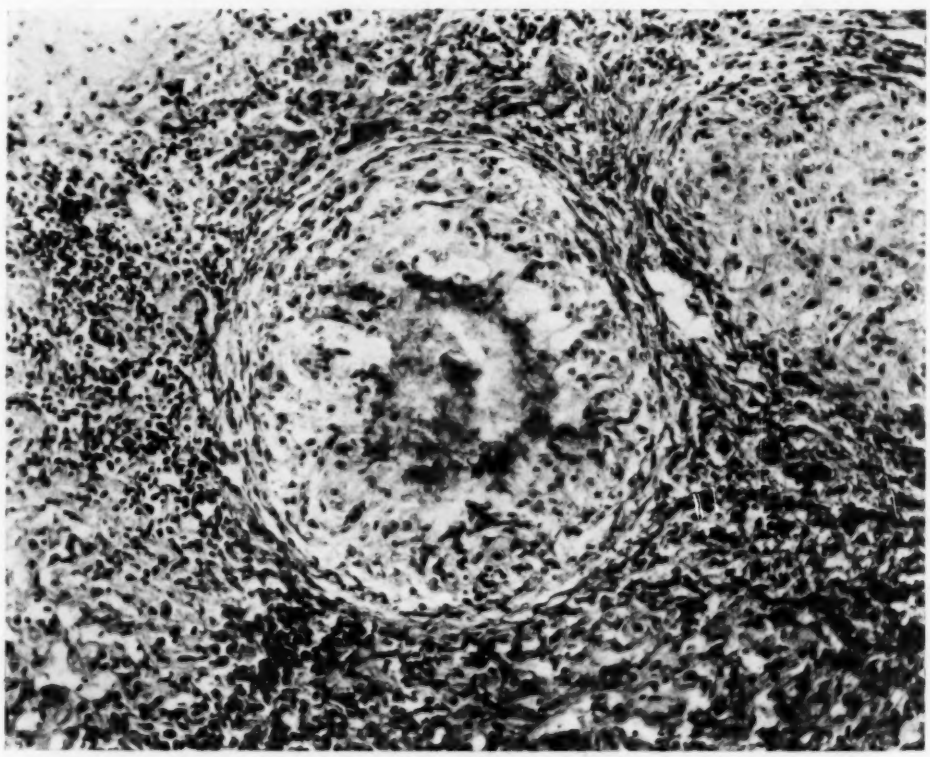

Fig. 11.—Solitary tubercle (× 150) near the periphery of the cerebrum of a chicken. The same case is shown in figure 3. The animal was killed 119 days after an intracerebral exposure to bovine tubercle bacilli. This figure may be compared with figures 6, 9 and 10.

assuming an epithelioid character and exhibiting a marked tendency to retain their follicle-like arrangement and to fuse to form conglomerate tubercles. They are also characterized by a definite attempt to become encapsulated, and in the older lesions by a peculiar hyalin-like degeneration of the center of the tubercle (fig. 11). I have failed to observe in chickens, even in those spontaneously affected with the avian organism,

the atypical or neoplastic-like lesions described by Chretien, Germain and Raymond.[5]

It also appeared from this study that, so far as the various mammals are concerned, the tuberculous process in the respective species studied was without significant differences regardless of the source of origin of the organism used to incite the lesions. This seems of significance and suggests the impossibility of one being able accurately to designate the bacillary type responsible for a given lesion on the basis of a morphologic study alone. It would seem that any differences of histologic detail assumed by the resultant reactions of tissue to the respective types of tubercle bacilli are determined for the most part by factors inherent in the host rather than by the possession by each of the three bacillary forms of certain lesion-inciting constituents which are specific for it. In this connection it is of interest to note that Fox, after a comparative study of tuberculous infection in the lower mammals and man, concluded: "The form of tuberculosis as seen in all animal groups is the expression of the peculiar characteristic reaction that each group presents to the infection," [6] and "individual peculiarity of an order, family, or genus must play a very large rôle in the inception, development, and result of tuberculous infection." [7]

These observations emphasize the indispensability of inoculation of an animal in every instance before one can definitely claim that a certain lesion has been caused by a given form of *Mycobacterium tuberculosis*. The designation of the bacillary type responsible for a given lesion can be made with certainty only when the results obtained from proper tests of pathogenicity are available.

SUMMARY AND CONCLUSIONS

With the use of pure strains of *Mycobacterium tuberculosis*, representative of the human, bovine and avian forms of the organism, experimental tuberculous infection was induced by various procedures in chickens, rabbits, guinea-pigs and dogs. From the lesions obtained a comparative study was made to determine whether the anatomic character of the cellular reaction in the respective species varied with the type of the tubercle bacillus used to incite the lesions, or whether the histologic character of the lesions in a given species was constant regardless of the form of tubercle bacillus present. From this study the following conclusions seem pertinent:

5. Chretien; Germain, and Raymond: Rev. de la tuberculose (s. 3) **4**:25, 1923.

6. Fox, Herbert: J. Am. Vet. M. A. **72**:792, 1928.

7. Fox, Herbert: Tr. Nat. A. Prev. Tuberc. **24**:199, 1928.

Variations in the character of the reaction of the tissue to *Mycobacterium tuberculosis* are not determined by the type of the organism per se, but by certain indefinite factors which are inherent in the species possessing the infection.

The histologic nature of tuberculous infection in a given species is essentially the same regardless of the form or of the origin of the particular strain of tubercle bacillus responsible for the lesions.

The lesions of tuberculosis in the common fowl usually possess certain anatomic characters that distinguish them from tuberculous lesions in the lower mammals.

These observations indicate that it would be injudicious to designate a given tuberculous infection as being due to organisms of human, avian or bovine origin in the absence of results of tests for pathogenicity.

SPONTANEOUS BILATERAL DECAPSULATION OF THE KIDNEYS

REPORT OF A CASE *

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AND
CARL W. APFELBACH, M.D.
CHICAGO

The kidneys described herein were removed from the body of a white woman, 35 years old, who died in the Presbyterian Hospital in March, 1930.

REPORT OF CASE

History.—Two years previous to death, the patient came to the hospital complaining of constipation, bleeding hemorrhoids and tenderness in the hypogastrium, all of these complaints being of several years' duration.

After an enema of barium and a roentgen examination that demonstrated a constriction of the colon, a diagnosis of carcinoma of the sigmoid portion of the colon was made. The neoplasm was removed, and a lateral anastomosis was made between the proximal and distal ends of the colon.

Nine months later, the patient returned to the hospital because of bleeding from the rectum. The previous anastomosis of the colon was resected, an abdominal colostomy was established, and the rectum was removed through the perineum.

In February, 1930, the patient again returned, complaining of loss of weight, bleeding from the opening produced by colostomy and nausea. The symptoms and physical observations were believed to result from metastases in the abdominal cavity and from partial obstruction of the bowel. The patient lived for one month, and during this period the predominating symptoms were prostration, anorexia and weakness. Only one examination of the urine was made. No albumin and no casts were found, and the specific gravity was 1.008. There was no clinical suspicion of renal insufficiency, and a chemical examination of the blood was not made.

Diagnosis.—The clinical diagnosis was: metastatic carcinoma of the colon proximal to the opening produced by colostomy; partial intestinal obstruction and secondary anemia.

The anatomic diagnosis was: long absence of the sigmoid portion of the colon and rectum; old colostomy; carcinomatous metastases in the periaortic and mesenteric lymph glands, in the pelvic peritoneum and in the ureters and periureteral adipose tissue; partial intestinal obstruction due to fibrous adhesions between the small bowel and the carcinomatous metastases; bilateral obstruction of the ureters, bilateral hydro-ureter and hydronephrosis; bilateral decapsulation of the kidneys; general anemia; marked emaciation and ulcers of the colon due to impacted fecal masses.

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Macroscopic Examination of Kidneys.—In the retroperitoneal space on each side there was a large, cystic mass; that on the right side weighed 1,060 Gm., and that on the left, 1,085 Gm. At the brim of the pelvis each ureter was invaded by gray, firm tissue like that in the peritoneal covering of the small pelvis. The periureteral adipose tissue was also firm and formed a hard encasement for the ureters to within a few centimeters of the renal pelves. Above the constriction of the ureters at the brim of the small pelvis, the walls were only slightly thickened, gray and opaque, and the average circumference of the lumens was 1.5 cm.

The fluid in each of the perirenal sacs was contained in a single cavity (fig. 1), and the fluid was watery and light yellowish brown. Attached to the lining of the sacs and the surfaces of the kidneys there were thin clots of blood, some of it brown and some of it reddish purple.

The alterations in the two sacs and kidneys were identical, so that only one kidney and the wall of the cyst will be described.

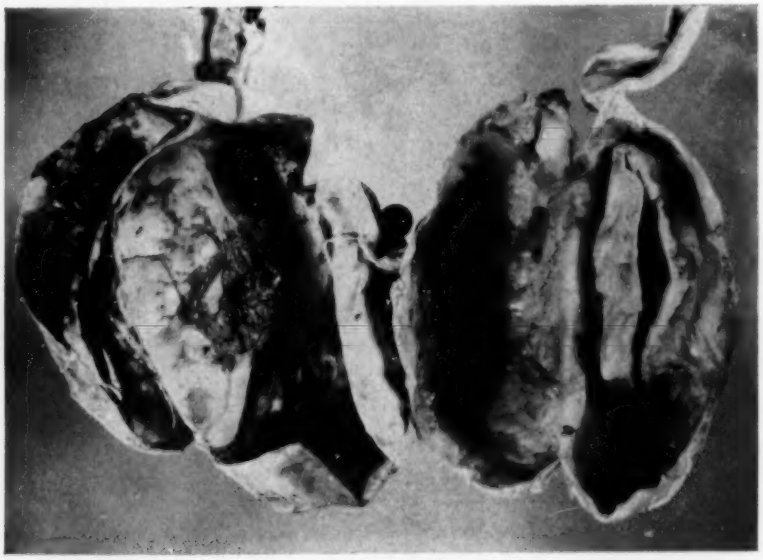

Fig. 1.—Photographs of the two kidneys after fixation in formaldehyde. The capsules have been cut open, thus exposing the two compressed kidneys. Clotted blood is adherent to the surfaces of the kidneys and to the linings of the sacs.

The wall of the cyst on the left side was flexible and translucent. Attached to the outside were adipose tissue and peritoneum, and at the superior surface muscle was firmly adherent. In its largest extent, the wall was of paper-like thickness, but at the thickest regions, where the kidney was embedded deep in the wall and where the diaphragm was attached, the wall was from 7 to 10 mm. thick.

The kidney was compressed by the fluid, so that its medial surface was flattened against the wall of the sac for from 1 to 2 cm. from the hilus. The junction of the lining of the sac with the surface of the kidney appeared to be a continuous membrane. Slight manipulation of the kidney, however, loosened the two surfaces; the wall of the sac then could be traced to the junction of the renal pelvis with the kidney. At this junction (fig. 2) there was a wall of fibrous tissue that varied from a tissue paper-like membrane in a few places to a heavy, fibrous

band several millimeters thick, in most places. The material that sealed the medial surface of the kidney to the sac was gelatinous and gray.

The lumen of the renal pelvis was ovoid, and the calices were obliterated, in contradistinction to the usual type of hydronephrosis in which the calices are dilated and extend up into the kidney as saccules. The cavity of the renal pelvis was equivalent to about 50 cc. The wall of the renal pelvis was thin. In most places, the wall of the renal pelvis was firmly joined to the kidney, and the cavity of the sac was separated from the cavity of the renal pelvis by from 2 to 3 mm. of firm, fibrous tissue.

The surface of the kidney was smooth, and the capsule was transparent, so that grossly it appeared as if the renal substance were bare. The renal parenchyma was light brown, glistening and bloodless. In cut surfaces, the cortical and medullary markings were regular and distinct.

Microscopic Examination of Kidneys.—In sections of the wall of the cyst, made from several regions, there was an abundance of young fibrous tissue. Infil-

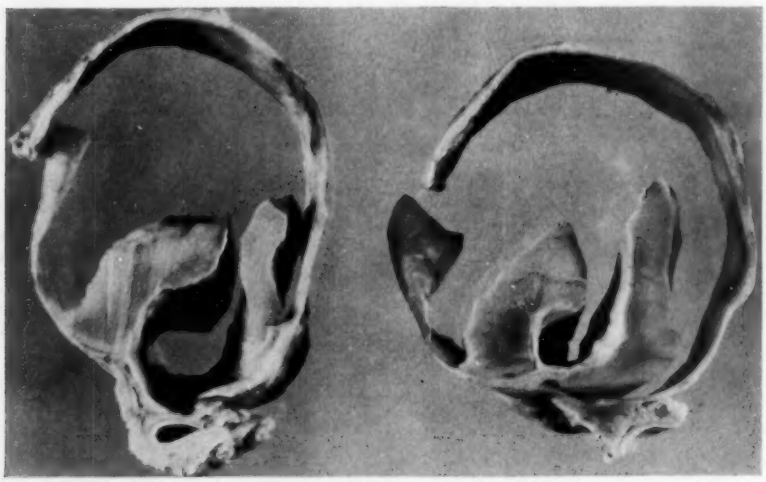

Fig. 2.—Coronal sections through the left kidney and the wall of the sac illustrate the ovoid shape of the renal pelves. In the section to the left the thinness of the wall between the lumen of the sac and the renal pelvis is demonstrated.

trations by round cells and new blood vessels were sparse. No distinct type of cell formed a lining. The inner layers of the wall appeared to be edematous. In a few regions, where there were gray plaques in the peritoneal covering, carcinomatous metastases were present.

The alterations in the kidneys were slight. The interstitial tissue, particularly of the medulla, was widened, but there was no increase of cells. Near some of the larger blood vessels at the junction of cortex and medulla, and also beneath the capsule of the kidney, there were spaces surrounded by fibrous tissue that contained a homogeneous, eosin-staining material. Covering the kidney, there was a fibrous capsule made up of several layers of fibrous tissue.

In the fat about the ureters, there were abundant metastases. The epithelial cells were arranged in solid masses of from 10 to 50 cells, and in a few places formed alveoli.

In sections through the pedicle of the kidney there was no evidence of metastasis.

Histologic Diagnosis.—The histologic diagnosis was: adenocarcinomatous metastases in the wall of the ureters, in the periureteral adipose tissue and in the peritoneum covering the perirenal cyst; dilated lymph spaces between the capsule of the kidney and the kidney itself and also in the renal parenchyma.

COMMENT

In the medical literature there are only a few reports of accumulation of fluid in the renal capsule similar to that described here. The alterations that occur with decapsulation from hemorrhage of traumatic origin have been frequently described and are well known.

Except for two instances, fluid that collects in the renal capsule has been regarded as a serous exudate from an inflamed capsule or as lymph from a blocking of the lymphatic channels of the kidney and capsule.

The reasons in favor of interpreting the fluid as having an origin other than from urinary excretion are dependent on chemical examinations and the failure to find an opening between the renal pelvis and the sac outside of the kidney.

Thus far, three names have been applied to this anatomic alteration: perirenal hydronephrosis, perirenal hygroma and renis hydrocele.

Minkowski [1] had the opportunity of investigating the characteristics of the fluid in a perirenal cyst of this type during the lifetime of the patient. A cystic mass, thought to be a hydronephrosis, was observed in the right side of a young man, and fluid was aspirated. This fluid and the urine did not have the same chemical composition, and therefore certain experiments were performed to determine whether or not the composition of the aspirated fluid could be changed with alteration of the chemical components of the urine.

The patient was fed benzoic acid. Hippuric acid appeared in the urine, but not in the cystic fluid. Large doses of methylene blue were administered by mouth. The fluid in the sac became slightly tinged, but not with the same intensity of blue that appeared in the urine. The excretion of urine by the kidney was of normal amount, but nevertheless the sac refilled rapidly after aspiration.

The kidney and its external cyst were removed. In gross relationship of kidney and perirenal hydronephrosis the specimen was similar to ours, except that there was no true hydronephrosis. There was no opening between the renal pelvis and the external sac. Minkowski believed that the fluid was of lymphatic origin due to stasis within the kidney. A thin capsule was present on the surface of the kidney, but he inferred that this had formed after the original space had developed.

1. Minkowski, O.: Mitt. a. d. Grenzgeb. d. Med. u. Chir. **16**:260, 1906.

In other words, the fluid in the subcapsular space was a retrograde flow of lymph from the kidney into the true subcapsular space.

Similar specimens have been reported on by Lipschutz,[2] Hildebrand,[3] Connerth,[4] Coenen and Silberberg,[5] Malherbe,[6] Kirmisson,[7] Good,[8] Krogius[9] and Löwenstein.[10]

Lipschutz and Coenen and Silberberg concurred with Minkowski in holding that the fluid outside of the kidney had its origin from lymph. They believed, however, that the fluid collected within the capsule of the kidney, thus splitting the capsule into two layers.

Hildebrand, because of a bloody fluid in the cyst that he described, and also because of a history of trauma to the patient, believed that a hemorrhage had occurred first, and that subsequently a serous fluid collected. Malherbe also subscribed to this explanation in reporting his case.

In the kidney described by Good, there was a tract between an internal hydronephrosis and the sac outside of the kidney. Kirmisson also believed the fluid in the perirenal space to be of urinary origin, even though he was unable to demonstrate a connection between the renal pelvis and the sac outside of the kidney.

Others have ascribed inflammation of the capsule of the kidney as the cause of the perirenal subcapsular collection of fluid.

In our case, at the time of the autopsy, it was assumed, because of the constriction of the ureters by carcinomatous metastases, that the collection of fluid outside of the kidneys was due to extravasation of urine. The two specimens were viewed from the standpoint of valuable material for a museum rather than with the knowledge that there existed in the literature the conception of lymph stasis as the probable cause.

The chief purpose in presenting the material, therefore, is to demonstrate an unusual disease of the kidney and its capsules.

There is some evidence to support each of the two views, namely, that the fluid is lymph and that the fluid is extravasated urine.

There is no blocking of the lymph channels of the renal pedicle by carcinomatous metastases, and it is through the pedicle that most of the lymph is drained from the kidney and its capsule.

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2. Lipschutz, B.: Ann. Surg. **81**:502, 1925.
3. Hildebrand, O.: Arch. f. klin. Chir. **130**:337, 1924.
4. Connerth, O.: Ztschr. f. urol. Chir. **11**:169, 1923.
5. Coenen, H., and Silberberg, M.: Beitr. z. klin. Chir. **130**:374, 1924.
6. Malherbe, A.: Ann. d. mal. de org. genito-urin. **8**:268, 1890.
7. Kirmisson, M.: Rev. de chir. **19**:825, 1899.
8. Good: M. & S. Rep. **24**:287, 1871.
9. Krogius, A.: Finska läk.-sallsk. handl. **63**:493, 1921.
10. Löwenstein, E.: Berl. klin. Wchnschr. **57**:1177, 1920.

In some regions, the renal pelvis is separated from the perirenal sac by a tissue paper-like membrane through which one can conceive that urine could filter.

The disease was bilateral and symmetrical. In view of this characteristic, one must bear in mind that there may have been a congenital anomaly in the development of the renal pelvis at its junction with the kidneys. Obstruction of the ureters, with and without carcinomatous infiltration of the lymphatics of the ureter and renal pedicle, is common, yet large collections of fluid in the renal capsule are rare.

The fluid in the perirenal sacs was watery and did not coagulate in fixing fluid.

SUMMARY

Two kidneys with a watery fluid in their capsules are described. The names commonly given to this condition are perirenal hydronephrosis, perirenal hygroma and renis hydrocele.

In the cases of accumulations of fluid in the capsules of the kidneys thus far reported in the literature the accumulations are explained by the authors as collections of lymph from blockage of lymph channels, as exudates from inflammation of the renal capsules, or from hemorrhage, and as extravasations of urine.

The gross and histologic evidence in our case points as much to extravasation of urine within the capsules of the kidneys as it does to blockage of lymph channels. The alterations in the capsule are those of encapsulation, and inflammation seems to be a remote etiologic explanation.

Laboratory Methods and Technical Notes

A RAPID AND PERMANENT METHOD FOR STAINING MYELIN SHEATHS *

CYRIL COURVILLE, M.D.
AND
ARAM KRAJIAN
LOS ANGELES

The study of myelinated nerve fibers from the standpoint of pathologic changes, as well as from that of their normal structure and distribution, has been complicated by the length of time required by the various technical methods devised for their successful demonstration. The modifications of Weigert's original method, as well as others more recently described, require considerable time, and often the results leave much to be desired. Weil [1] recently devised a rapid method which serves a useful purpose, although in our hands, it has failed to demonstrate individual fibers as well as we should like. We have devised a method which seems to have many of the advantages of the longer methods, as far as the results obtained are concerned, and yet can be completed in thirty minutes. This is of special value in making a rapid diagnosis of questionable cases in which systemic disease of the spinal cord is suspected. The pathologist may have a section for study by the time he has completed the postmortem examination, for preparations from fresh tissue can be made in even less time than that stated. The stain is permanent, as far as can be determined, for we have well preserved sections that were made over a year ago. The details of the fibers are fairly sharp and clear, although not stained as deeply as in the longer methods.

METHOD

Hardening.—For rapid diagnosis on fresh tissue, boil the blocks for one minute in 10 per cent formaldehyde and then leave in the same solution in a paraffin oven for five minutes before cutting frozen sections. When the section is not demanded in a short time, fix the tissues in 10 per cent formaldehyde for twenty-four hours or longer.

Sections.—Cut frozen sections 10 microns thick. Receive sections in a large dish containing tap water.

Mounting.—Draw sections on to slides and let the excess water drain off for about a minute and dehydrate with absolute alcohol, pouring on a few drops two or three times, each time allowing it to evaporate. Blot and dip the slide in a thin

* Submitted for publication, Dec. 19, 1930.

* From the Department of Pathology, Los Angeles County General Hospital.

1. Weil, Arthur: A Rapid Method for Staining Myelin Sheaths, Arch. Neurol. & Psychiat. **20**:392, 1928.

celloidin solution fixing the section to the slide. Dip the slide in tap water for a few seconds.

Mordanting.—Cover the section with 15 per cent hot aqueous solution of ferric chloride [2] for five minutes. Drain the solution from the slide. Do not wash.

Staining.—Cover section for five minutes with equal parts of hematoxylin solution [3] and distilled water, heated to 60 C. This stains the section extremely black.

Washing.—Wash thoroughly in tap water.

Destaining.—Remove excess stain in a 1 per cent aqueous solution of ferric chloride, dipping the slide in and out of the solution until the gray matter begins to appear in contrast to the dark medullary substance. This takes place in from ten to twenty-five seconds.

Washing.—Wash the slide quickly in tap water.

Differentiation.—Cover the section with a 0.25 per cent aqueous solution of potassium permanganate and shake with the fingers to secure even differentiation, which takes place in about five seconds. This step should be controlled under the microscope.

Washing.—Thoroughly wash the section in tap water.

Dehydration.—Remove water from the section after draining off the excess by pouring on a few drops of absolute alcohol and draining off, repeating three or four times. Blot between filter paper.

Clearing.—Plunge section in a container of equal parts of aniline oil and xylene for about three minutes and then in xylene for another three minutes.

Mounting.—Mount in Canada balsam or gum damar.

This method consists essentially of a staining of the myelin sheaths with hematoxylin after mordanting in ferric chloride solution.

The use of hot solution hastens the process and makes it adaptable for rapid diagnosis. The important steps are the removal of excess stain with a 1 per cent aqueous solution of ferric chloride and differentiation in 0.25 per cent aqueous solution of potassium permanganate. If, in the process of differentiation, the black color is too intense, the sections should be destained a little longer in the ferric chloride solution. The process of differentiation serves two other purposes, that of counterstaining the gray matter and degenerated areas a golden yellow and that of checking the action of ferric chloride. This insures the preservation of the stain in the myelin sheath, making a permanent preparation. If after differentiation it is found that the yellow counter stain is not deep enough, the potassium permanganate solution may be added again and the slide shaken for a few additional seconds.

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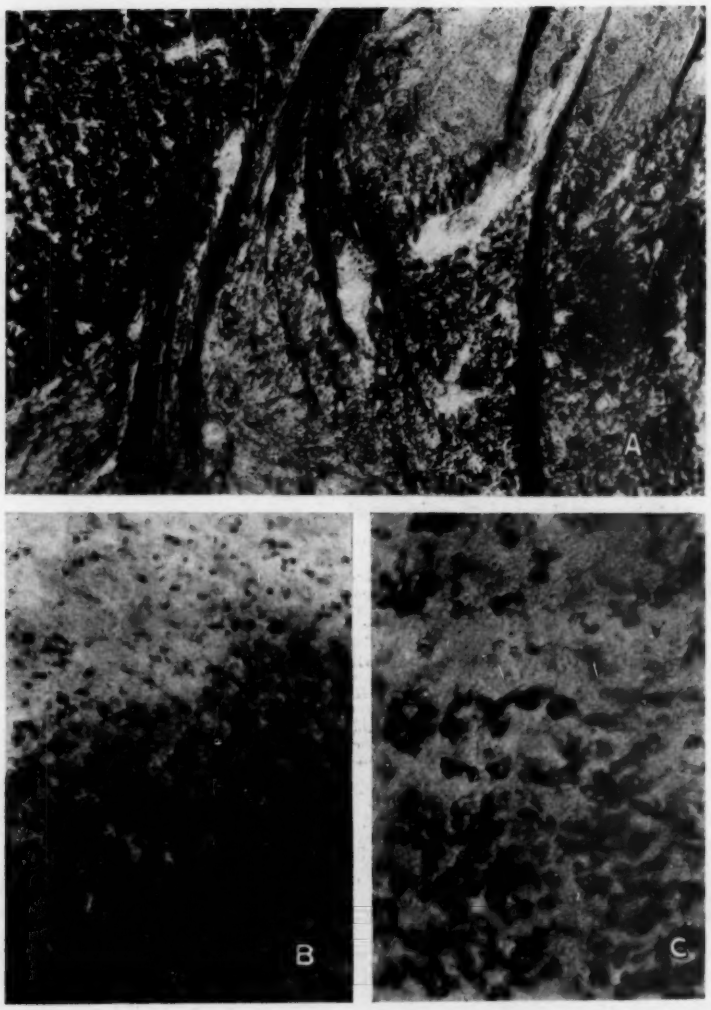
2. Ferric chloride solution should be made up fresh each time. Dissolve 15 Gm. of ferric chloride in 100 cc. of hot tap water and raise the temperature to 60 C. just before use.

3. Hematoxylin solution is prepared by dissolving 10 Gm. of hematoxylin crystals in 90 cc. of absolute alcohol and ripening in an incubator at 37 C. for two or three weeks. This solution is stable and will keep for months.



A, myelinated fibers entering the posterior horn of the spinal cord. The method shows them as clearcut fibers in longitudinal section and as well defined rings in cross-section; × 100. *B*, degeneration of the myelin sheaths of the subcortical white substance in a case of encephalitis periaxialis diffusa (Schilder's disease) as demonstrated by the method; × 230. *C*, degeneration of myelin sheaths of nerve fibers at the margin of the fasciculus gracilis in a case of tabes dorsalis; × 230.

The interpretation of the results is the same as in the Pal-Weigert method. The myelin sheath stands out as a ringlike structure surrounding the unstained axis cylinder core as seen in the cross-section. In longitudinal section, it appears as a light-bluish strand, observed characteristically in the gray matter of the cord (see figure, *A*) and the deeper layers of the cerebral cortex. The accompanying illustrations show the details emphasized by the method. In rapid degenerations the myelin is seen to be broken up into globules in the course of the nerve fibers (*B*). If the process is a slower one, as in tabes dorsalis, the typical shrinking and distortion of the fibers may be seen (*C*).

The method seems to be best adapted for frozen sections, for we have had poor results on paraffin sections of formaldehyde-fixed material. No results were obtained on tissues fixed in Zenker's fluid.

General Review

REVIEW OF SOME RECENT BOOKS ON BACTERIOLOGY

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Even in the biologic sciences, "of making many books there is no end." There are, however, peculiar periodic rises and falls in the tide of book-making. Granted the constant possibility of publication, the meaning of these ups and downs in the printing of volumes could be determined with assurance only after an examination of all the complicated factors influencing intellectual activity and its expression. Without making such a profound analysis, it may be said that one source of influence is certainly the stage of development of a science. It would, in the first place, be incorrect to suppose that the absence of book-making indicated stagnation in a science. On the contrary, book-making in a science is apt to decrease during periods of intense explorative investigation, when real beginnings are being made. After that period, the publication of volumes setting forth the newly acquired knowledge marks a sort of official opening of the new era. A second stage of relative stability in a science is often marked by the publication of numerous volumes, either as encyclopedic summaries of collected knowledge or as the exposition of a hypothesis drawn from many singular instances. A third stage also, a stage of stagnation, may be remarkable for the publication of numerous monumental volumes expressing the final doctrines of accepted authority.

At least two influences obscure these relationships of the publication of books to the stages of development of a science. The first of these is the irregularity of activities within the domain of the science. All stages from exploration to stagnation may occur at one time, and introductory books will be published simultaneously with the volumes of encyclopedias and documented dogma. The second influence obscuring this relationship is that exerted by the increase in journals. In earlier times, before there were many journals, publication of original observations in a volume was frequently the first means of dissemination of new knowledge. In more recent times, the increase in journals gives the author the means of publishing as separate articles the papers

that in other days he would have assembled first in a book. Finally, the accounts of some experiments, filling all the hundred or more pages in a single issue of a journal, are so voluminous that they should in reality be regarded as books.

During the past five years, there has been an extraordinary increase in the making of books in the science of bacteriology. These books represent all stages of activity in this field. Few or none may be said to express the absolutism of authority, because no one dares to assume authority in these days of incessant critical experimentation, because dogmatism is unfashionable, or because most textbooks contain a sufficiency of dogmatism more or less subtly intruded through an author's subconscious bias or point of view. Many of these books are stimulating for their new conceptions, and many are extremely valuable as sources of reference. Indeed, the bacteriologist has never before been so thoroughly supplied with literary tools for excavation and construction in his fields. It would be profitable to attempt to review and classify all of these books. They are so numerous and varied that a book about books, like Dible's recent monograph, "Recent Advances in Bacteriology," would be required to do justice to all of them. But the reviewer has little more than titular acquaintance with many of them, and is forced by limitations of knowledge and occupation to restrict his review to brief comments on a few books that he has read or consulted.

The rapid extension of bacteriology, its extraordinary utility and the segregation of workers intensely occupied in different parts of the domain have caused the publication of infinitely detailed reports on special regions with little or no coordinated description of the whole. Therefore there is no encyclopedia of bacteriology. While these special publications have great value, it is to be regretted that there is no systematic treatise on the whole field of bacteriology. The longer such a publication is delayed, the longer will each bacteriologic specialist continue to behave as if the bacteria were unique micro-organisms of his province. This attitude has and will continue to hinder the development of a unified general science of microbiology.

In the medical field, the great encyclopedia of bacteriology has been the "Handbuch der pathogenen Mikroorganismen," which Kolle and Wassermann began to publish in 1902. During the past four years, Kolle, Kraus and Uhlenhuth, as editors, have been issuing the fascicles that will compose the ten volumes of the third edition of this "handbook." Each volume contains 1,000 or more pages. At this date, nine of the volumes are complete, while only two sections of the third volume and the general index remain to be issued. The whole work is the product of the labors of more than 150 authors.

An attempt at coordination has been made occasionally, but each chapter is in reality an independent monograph by a specialist in that subject. With a few notable exceptions, the authors are German or Austrian. This, undoubtedly, has some influence on the point of view and the use of foreign literature. In spite of it, however, most of the chapters show an unusual breadth of treatment and an attention to important articles in English, French and American journals. The plan of this great work has been to cover the whole field of microbiology and the disciplines closely related to it—immunology, serologic diagnosis, serotherapy and chemotherapy. Somewhat more than five of the ten volumes are given to bacteriology in nearly all of its phases. The chief emphasis is on the pathogenic bacteria. The short sections devoted to the bacteria of air, soil and water are largely technical and diagnostic. Large parts of several volumes are devoted to pathogenic fungi, spirochetes, viruses, protozoa and helminths. All the traditional aspects of immunology and serology are dealt with, and chapters, such as Landsteiner's on the lipoids, are allotted to the newer biochemical developments in immunology. It is impossible to review this encyclopedia in detail. It may be said, in general, that this third edition preserves the record of older knowledge and brings the summary of newer knowledge well up to date in most of the divisions of medical bacteriology. It is a huge storehouse of facts and suggestions. It is to be hoped that the greatest usefulness of the work will be ensured by the publication of a really good index.

A great compendium of modern knowledge of medical bacteriology is being published in the English language by the Medical Research Council of Great Britain. This work, entitled "A System of Bacteriology in Relation to Medicine," is to be issued in nine volumes, of which volumes 1, 2, 3, 4, 5, 6 and 7 have appeared. This "system" is said not to be an encyclopedia, but a comprehensive survey of the present knowledge of bacteria, spirochetes, filtrable viruses and pathogenic fungi with special regard to their relations to various fields of medicine. It is frankly a system of medical bacteriology, with "short reviews of those economic applications of bacteriology which have special interest for the medical worker." This "system" will be the assembled contributions of nearly 100 British bacteriologists, each a specialist in the subject about which he writes. Unequal treatment and some unsystematic arrangements result from the separate endeavors of a multiplicity of authors. But in this work there is abundant evidence of the coordinating activities of skilful and learned editors. The quality of the volumes has exceeded the high expectations excited by the prospectus of the work. There is no work comparable to this "system" in the English language, and I think that no other treatise on modern bac-

teriology is its equal. Throughout the work, there is a manifest interest in the bacteria themselves. In fact, the whole of the first volume is given to considerations of bacterial morphology, bacterial metabolism, growth and reproduction, life cycles and variation. Even in the other volumes dealing with the relationships of bacteria to specific diseases of man, animals, plants and insects there is a continued focusing of attention on the essential characteristics of the micro-organisms. Volume 6, which has just appeared, is devoted chiefly to a systematic consideration of immunology, which, however large its own independent serologic scope may be, remains indissolubly attached to bacteriology. It would be difficult to overstate the value of this work. English and American bacteriologists and the bacteriologists of other countries will for a long time owe a debt of gratitude to the Medical Research Council for the publication of "A System of Bacteriology in Relation to Medicine." At present, while many are profiting by the unindexed volumes, they are hoping that the final publication of a detailed index will give them further cause for thankfulness.

Next to these comprehensive, semi-encyclopedic works, come the textbooks of bacteriology as sources of instruction for the novice and as sources of reference or of controversy for the specialist. Most of the commonly used American textbooks of bacteriology have been revised and issued in new editions during the past few years. The recent editions of Zinsser's "Text-Book of Bacteriology," of the book on "Pathogenic Microorganisms" by Park, Williams and Krumwiede, of Kendall's "Bacteriology" and of Jordan's "General Bacteriology" have brought these books as nearly up to date as the thoroughness of the revisers and the exigencies of publication permit. It is remarkable that textbooks dealing with the same general material should be as different as these books seem to be. They are, after all, a reflection of the interests and experience of their authors. Each book has its excellences and defects, and all suffer from the impossibility of cramping bacteriology, immunology and serology, medical mycology, virology and sometimes protozoology between the covers of one volume of from 700 to 1,000 pages. In my opinion, Zinsser's book is to be preferred for its treatment of bacteria in relation to disease, the Park, Williams and Krumwiede book for its description of practical technical procedures and some aspects of public health bacteriology, and Kendall's book for its chemical and metabolic considerations. A newcomer in this group is the "Text-Book of Bacteriology" by W. W. Ford, published in 1928. The special feature of this book is the systematic description of the characteristics of a great number of bacteria and other organisms—micro-organisms of air, soil and water, as well as micro-organisms of medical importance. The spirochetes, rickettsiae

and filtrable viruses are included in the descriptions, and the book contains chapters on infection, immunity and serology. Its closely printed pages, which number 1,000, contain a wealth of recorded observations, and its illustrations, many of them drawings, are refreshingly new. It seems likely that this book will prove of more value to the systematic bacteriologist than to the beginning student.

The latest textbook in the field of medical bacteriology deserves separate consideration in recognition of its individual excellence. This is the two volume work, "The Principles of Bacteriology and Immunity," by Topley and Wilson, published in 1929. The book grew out of the experience of the authors in attempting to provide adequate training for men and women who required a larger course in bacteriology than that given in medical schools in England. The authors attempted, as they have stated, to provide a "text-book which will be of service to those students of medicine and biology who wish to make a serious study of bacteriology and its application to the problems of infection and resistance." They have succeeded admirably in writing the first really comprehensive textbook of medical bacteriology in the English language, in providing students of biology with an adequate treatise on medical bacteriology and in giving medical students a biologically conceived textbook of appropriate bacteriology. In order to accomplish this, the authors required the space of two volumes with a total of about 1,300 pages and were forced to omit all detailed description of technic. The descriptions of technical procedures, which vary from one laboratory to another, are easily supplied in manuals. It seems to me well to free a book from these encumbering descriptions, and I judge from the reception of this book by my associates and students that appreciation of its merits has not been decreased by the absence of the usual pages on technic. Each volume is divided into two parts. In the first part of volume 1, the general characteristics of bacteria are described and discussed in the light of modern discoveries. The second part of the first volume is given to systematic bacteriology. In this section, succinct detailed descriptions of many micro-organisms, chiefly pathogenic bacteria, are provided. The descriptions include also organisms of the azotobacter group and other nonpathogens. Spirochetes, filtrable viruses and rickettsiae are considered here so far as specific knowledge of them permits description. Mycology is not dealt with. The terminology used is the nomenclature, occasionally modified, recommended in the 1920 report of the first American Committee of the Society of American Bacteriologists. Volume 2, part 3, deals with infection and resistance, immunology and serology. Volume 2, part 4, devoted to the application of bacteriology to medicine and hygiene, contains concise descriptions of important infectious dis-

eases of man and animals and of the most significant bacterial phenomena associated with these diseases. There is so much to praise in these volumes that a review might well become an abstract of the book. The intelligence, the critical biologic point of view, the conciseness of style and the choice and arrangement of material shown in this book give it qualities outranking any other book of its kind known to me.

The knowledge of the physiology, metabolism and biochemistry of bacteria has been collected and systematized in several unusual books published during this period. The most comprehensive of these is the three-volume work, "The Physiology and Biochemistry of Bacteria," published in the period 1928-1930 by Buchanan and Fulmer. These volumes are an exposition of the analysis of bacteriologic data by methods of physical chemistry and mathematics. It is amazing to the medical bacteriologist to find that so many bacterial phenomena lend themselves to investigation by these methods and to see in these books so much evidence of the rational physical chemical and biochemical trend in the science of bacteriology. The first volume deals mathematically and descriptively with curves of growth, the phenomena of reproduction and the energetics of cells. The second volume is given to the effects of environment on bacteria and the third to the effects of bacteria on environment. The chemist has criticized these books as being abbreviated compendiums of texts in physical chemistry. The bacteriologist, however, will find this an assistance rather than a hindrance. Throughout, the authors have been concerned with the application of physics, chemistry and mathematics to the understanding of bacterial phenomena. On first inspection, these books appear to have little direct bearing on medical bacteriology. But any one who wishes to see medical bacteriology escape from the fetters of a diagnostic aid knows that its scientific advancement must take off from the fundamental knowledge presented in such books as these.

Somewhat similar material has been handled by Stephenson in a single volume, "Bacterial Metabolism," published in 1930 as one of the Plimmer series of "Monographs on Biochemistry." The author has stated in the preface that the aim of her book "has been to choose from the mass of data on the chemical activities of bacteria facts which may help us gain an insight into the essential chemical processes accompanying the life of the organisms concerned." She voices an opinion, fervently held by many, that it is time to "appraise our knowledge of bacteria as living organisms apart from their rôle as disease germs or the bearers of commercially important catalysts." Of course, all of the significant fundamental knowledge of these organisms will in the end be turned to the service of man and animals. Yet it is delightful for the broadly interested bacteriologist to find such a book

as this one written with an avowed interest in the bacteria for themselves. It is additional evidence that the time is nearly here when a refutation will be provided for Lord Balfour's statement that "though the bacteria are the subject matter of bacteriology they do not, in and for themselves, constitute its main interest." Chapters in this book deal with energy relations and fermentation, respiration, growth and nutrition, the breaking down of carbohydrates, and synthesis, the breaking down of proteins, nitrogen fixation and autotrophic bacteria. The book has the fine scientific qualities of the monographs of this series.

A great service has been rendered to "all bacteriologists in all bacteriological laboratories" by the publication in 1930 by Levine and Schoenlein of "A Compilation of Culture Media for the Cultivation of Microorganisms." In this huge book, with pages printed in double columns, the formulas of about 7,000 culture mediums have been brought together, classified into groups and subgroups, and so arranged and catalogued under keys and indexes that the matter dealing with any sort of medium and the food requirements of any sort of bacterium may be found with ease. The book was prepared at the request of the Society of American Bacteriologists and financed by a grant from the Digestive Ferments Company. It is a monument to the industry of the compilators and their systematic minds. If so many kinds of culture mediums are needed by bacteria, the conclusion must be drawn that these organisms have extraordinarily fastidious food requirements. On the other hand, there is the distinct possibility that the multiplicity of minor variations of certain basic mediums is more indicative of the uncontrolled vagaries of bacteriologists than of the specialized appetites of the bacteria. Perhaps the book will serve to curb the invention of new, but unnecessary, culinary mixtures and, while providing a mine of useful information, help to stabilize the use of cultural substrates.

A small, but serviceable, companion to this compendium of culture mediums and a book with merits of its own that will appeal to the medical bacteriologist, as well as to the biochemist and industrial bacteriologist, is the "Index to the Chemical Action of Microorganisms on the Non-Nitrogenous Organic Compounds," published in 1930 by Fulmer and Werkmann. The material is so arranged that it is possible to find in this book under the name of an organism, the products produced from various substrates; under the name of the product, the organism and the substrate to be used to obtain the desired substance, and under the name of the substrate, the products produced from it by various organisms. Authorities and references are cited for each statement. "Industrial Bacteriology," by Smyth and Obold, is another

book produced in 1930 showing how far the domestication of the bacteria has progressed.

In an attempt to present timely summaries of the "latest results of investigations in various lines of bacteriology and immunology," Jordan and Falk, in 1928, brought out a collection of contributions from 82 authors under the title, "The Newer Knowledge of Bacteriology and Immunology." By promptness in editing and publication the book escaped the delays that cause so many textbooks to be partially out of date by the time they are issued. The knowledge in it is in many cases sufficiently new and authoritative to serve the needs of future textbooks. As may be expected from multiple authorships, the treatment of subjects is uneven, sometimes overlapping and sometimes contradictory. On the whole, I have found it a useful and stimulating book, as have others with whom I have been associated. References to various chapters in it in recently published papers indicate that as a compendium of modern knowledge in medical bacteriology and immunology it has been of general service to investigators.

Since the decline of the influence of Pettenkofer, less attention has been paid by medical bacteriologists to the relation of the soil to outbreaks of disease in man and animals. As a source of spore-bearing anaerobes, however, the soil plays a predominant rôle in the gas gangrene and tetanus of man, in botulism and in a number of other infections of man and animals. It has important connections with typhoid fever, anthrax and possibly actinomycosis. It harbors numerous micro-organisms that harmfully or beneficially affect the plants on which human beings and animals subsist. In addition, the scientific medical bacteriologist cannot afford to neglect the knowledge of bacteria gained from the study of the micro-organisms of the soil. Therefore, it is appropriate to mention in this review the "Principles of Soil Microbiology" by S. A. Waksman, published in 1927. In this compendium, chapter 30 summarizes the knowledge of the soil as a habitat for micro-organisms causing diseases of plants and animals. Recent investigations of enzymes from a micro-organism of the soil inimical to the pneumococcus indicate that this field is certain to have an even closer relationship to medical bacteriology.

If any books might be expected to exhibit the true stage of development or the degree of stability of a biologic science, these should be the volumes on classification and nomenclature of the organisms with which that science deals. In bacteriology, the chief book on taxonomy is "Bergey's Manual of Determinative Bacteriology," the third edition of which was issued in 1930. A first glance at this book gives the impression that a vast number of bacteria are classifiable, and that bacteriologists have an acceptable system of classification. But those

who have seen this book grow and change under their eyes during the past few years and those who seek to place an organism by matching its characteristics with the descriptions in Bergey's manual know that while the book reflects a moderate degree of stability in bacteriologic taxonomy, it gives evidence also of a large and shifting uncertainty in bacteriology. The manual is, in fact, a body of unofficial suggestions. Its nomenclature is not acceptable to the majority of bacteriologists, and in some cases the grouping of micro-organisms seems to violate their natural relationships. Nevertheless, the manual is an invaluable source of information. As taxonomy must change with changes in knowledge, as many descriptions of bacteria are incomplete, and as most medical bacteriologists perpetuate confusion by their incorrigible laxity in taxonomic practice, a final and generally acceptable classification and nomenclature cannot be expected at this time. A recent addition to the English literature of this subject is the translation from the German of the two volumes of "Determinative Bacteriology" by Lehmann and Neumann. The translation has been made by Dr. Robert S. Breed and several associates. Since this book contains a certain amount of material on spirochetes, protozoa and fungi and on immunologic reactions, it might be placed among the handbooks of microbiology. It is appropriate, however, to review it in this paragraph dealing with the recent literature on taxonomy. Its main interest and "most permanent value," as Dr. Breed has remarked, "lies in its systematic arrangement of our knowledge regarding the still too imperfectly known and numerous types of bacteria," and in the classification and nomenclature used by Lehmann and Neumann. A distinct service has been rendered English-reading bacteriologists by making readily available this important expression of an authoritative German point of view. In addition, these volumes will serve as a valuable work of reference on the technical, biologic, taxonomic and historical matters that interest bacteriologists perennially. Finally, there is at present a renewal of the attempt to find some generally acceptable taxonomic scheme and nomenclature in bacteriology. Committees of the International Society for Microbiology and of the International Botanical Congress have been appointed to study these questions and to formulate a plan of concerted action. This book is awaited with high expectations.

The increasing knowledge of bacterial variation is apt to make the ways of most bacteriologists, especially the taxonomists, difficult for awhile. In the end, however—years hence—bacteriology will find simplifications and rationality in coordination of the completed studies of the variants and of the life cycles of the bacteria. The subject of variation in bacteria still lacks its comprehensive book. It is to be

hoped that one will be produced, gathering together all the reports of sound investigations that have been going on through many years. A great deal is already known of many phases of bacterial variability, from variations in colonies to variations in cells, from variations in metabolism, virulence and toxigenicity to variations in antigenic disturbances, from such hereditary changes as those described by Mellon, Löhnis and Almquist, to changes that might be interpreted as evidence of the life cycles of bacteria. The accumulated mass of evidence has broken down the unbiologic convention of fixity of form and of other characteristics and restored a biologic outlook on the capacity that bacteria have in common with other living things to change in response to external and internal influences. All of these new studies are of great importance to the medical bacteriologist and epidemiologist, as they will explain more and more of the phenomena of infectious disease and elucidate some of the mysteries of epidemics. At the beginning of the period under review one of the most remarkable of the books on this subject was the "Bakterien-Cyclogenie" published in 1925 by Enderlein. In order to gain an insight into the meaning of most of the passages in this book, it is necessary for the reader to learn the large new vocabulary coined by Enderlein. It is difficult to appraise the value of his observations of sexual phases in bacterial growth through "gonits," "spermits" and the cyclogenic stages consequent on the activities of the "mych," or ultimate nucleus, and the "mychit," or fundamental cellular unit. A great deal of new material can be found in this book. The phase of variation known as bacterial dissociation was studied exhaustively by Hadley, who begins his monograph on "Microbic Dissociation" with the statement that for the past three decades there has been accumulating an increasing mass of evidence pointing to the instability of bacterial species. After recording the results of experimental study of many of the conditions that bring about microbic dissociation, he points out that many of the important problems in modern bacteriology and pathology "have their roots in the phenomena of bacterial instability." In the course of this research, the bacteriophage was found to have such close and influential relationship to microbic dissociation that Hadley inclined to the view that both these reactions—transmissible lysis and bacterial instability—were "inseparably united in the reproductive mechanism of the bacterial cell." Bacteriophagic phenomena intensified the interest in filtrable viruses and the possibility of the existence of filtrable stages of bacteria. The latter subject has for a number of years engaged the attention of French bacteriologists. In 1929, Hauduroy summarized much of the knowledge of the filtrable forms of bacteria in his book, "Les ultravirus et les formes filtrantes des microbes." More recently, the

most exact account of experiments capable of demonstrating the filtrable forms of bacteria is the monograph published in 1931 by Hadley and his associates, describing their work, "The Filtrable Forms of Bacteria: I. A Filtrable Stage in the Life History of the Shiga Dysentery Bacillus." For the first time, bacteriologists have been provided with detailed descriptions of methods and procedures for obtaining filtrable stages of bacteria. This monograph is certain to stimulate much investigation in the attempt to substantiate or to disprove this most significant contention. The evidence thus far available seems to be most strongly in its favor. A more critical book dealing with morphologic variation in bacteria is Henrici's monograph, "Morphologic Variation and the Rate of Growth of Bacteria," issued in 1928. As a result of his laborious measurements of thousands of bacterial cells in various stages of growth, he found that the old monomorphic conception can no longer be considered sound, and should be modified. On the other hand, he concluded that the evidence for the existence of bacterial life cycles was inadequate to establish that conception. This field is now in a state of intense and fruitful cultivation.

The filtrable viruses, during this period, have received a very large share of the interest of all and the attention of a number of skilled investigators. Their medical and economic importance is so great that it is somewhat astonishing that really intensive study of them was delayed so long. At present, however, new methods of attack from the vantage points of methods of attempted cultivation and the analysis of inclusion bodies is rapidly extending the knowledge of these minute viruses. Two comprehensive books have been published on them. The first, in 1922, was the collection of special article under the title, "Filterable Viruses," edited by T. M. Rivers, and the second is the volume entitled "Filterable Virus and Rickettsia Diseases," by E. B. McKinley, published in 1929. Although a consideration of the rickettsiae is out of place here and really requires separate treatment in a special volume, these two books present most of the substantiated knowledge of the viruses.

So much of the research in bacteriology during this period has had its origin in the study of the phenomena of the bacteriophage that it is essential and appropriate to mention here d'Herelle's comprehensive book, "The Bacteriophage and Its Behavior," translated by G. H. Smith and published in 1926. The phenomena is so well known that a review of this book is unnecessary. The importance of the bacteriophage, whatever view one may hold as to its nature, is paramount in modern studies and in conceptions of the ultimate unit of vitality, the dissociation of bacterial species and the recovery from certain acute infectious diseases.

Medical mycologists see many apparently similar forms of fungi producing different diseases and many similar diseases produced by apparently different forms of fungi. The troubles seem to lie in the variability of the fungi under different conditions and the seeming impossibility of combining systematic mycology and clinical nosology in a workable classification. Two recent books in this field clarify some of the obscurities and darken others. The first of these, essentially a medical treatise, is the collection of the Adolph Germann lectures delivered by Castellani at the College of Medicine of the University of Illinois in 1926 and published later in book form under the title, "Fungi and Fungous Diseases." The book contains apparently concise descriptions of the fungi and the fungous diseases, is provided with tables for correlations and is well illustrated. It is, however, difficult for a student to establish identifications by means of this book. A broader and more "botanical" book is Henrici's "Molds, Yeasts and Actinomycetes," published in 1930, as a handbook for students of bacteriology. Most of the available knowledge of fungi is summarized in this book. It gives a valuable biologic insight into these organisms and more than fulfils the modest purposes of its author. Perhaps there are still too many uncertainties in this field to permit the publication of the sort of book for which the medical mycologist yearns.

Notable collections of the really vast accumulations of knowledge of the streptococci have been published during the past few years by D. and R. Thomson in the "Annals of the Pickett-Thomson Research Laboratory" of London. These annals are such large monographic treatments of the streptococci that they pass from the category of journals into the class of comprehensive books. In addition to presenting summaries of all the literature on the streptococci and on the relation of streptococci to scarlet fever, arthritis and rheumatic fever, the annals contain the results of photographic studies of the structure of the colony of these organisms on Crowe's medium, photographed by a special apparatus using ultraviolet light. The illustrations are superb. They do not convince me, however, that they are as significant as the authors think them to be for establishing the exact relationships among the streptococci. Much additional information is required, as is usual in any determinative bacteriologic procedure.

There is a definite tendency in these days to assign the spirochetes to the general class of bacteria. Whatever their nature, the medical bacteriologist is forced by occasion and interest to concern himself with these organisms. In this case again, he desires a comprehensive treatise. He has available numerous short summaries of the knowledge of the spirochetes. He will find a large store of facts in the book published by August Pettit, in 1928, as a "Contribution à l'étude des

spirochétidés." One whole section of this book is given to a consideration of the jaundice-producing spirochetes—especially *Spirochaeta icterohemorrhagiae*. Other sections deal with all the types of spirochetes and the technic of studying them. The book presents the results of nearly twenty years of investigation of the spirochetes by Pettit, who began his work with Laveran in 1911.

In many of the books mentioned in this review, the authors have, in one way or another, stressed the importance of veterinary medicine for human medicine. The study of pathogenic organisms should obviously include the bacteria that produce disease in animals along with those that produce disease in man. The liaison, however, has not always been as close as it should be. In deploring this fact, Topley and Willson write: "In no branch of medical science is the sterilizing effect of the anthropocentric attitude more obvious than in the study of bacterial infection." This implies that almost too much study by man has been devoted to the infections of mankind. A closer relationship between human and veterinary medicine is being voluntarily sought by the intelligent medical bacteriologists and forced by the episodes of undulant fever, tularemia and a number of diseases common to man and animals. The most recent correlative book on this subject is the small volume, "Diseases Transmitted from Animals to Man," published by T. G. Hull in 1930. It is a useful book as far as it goes, and is good enough to stimulate the wish that the author would enlarge it in the next edition.

It has been necessary to omit from this review the mention of many books, both foreign and American. Enough has been written, however, to record the extraordinary activity in bacteriology that has been characteristic of the past five years. If there has been no end of making many books, this has been due to the limitless material from which to make them.

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Paleopathologic Report

OSTEITIS FIBROSA IN A SKELETON OF A PREHISTORIC AMERICAN INDIAN*

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In an attempt to understand prehistoric American Indian life one must consider not only the cultural aspects, such as artefacts and type of burial, but also the pathologic conditions encountered. Anomalous or pathologic conditions are in themselves sufficient to modify the existence of an individual. An unusual example of a pathologic condition was excavated by the University of Chicago Archaeologic Survey, from mound F14, Fulton County, Lewistown, Ill., during the summer session of 1930.

The skeleton is that of a man approximately 35 years old. He was a cripple with an affliction involving practically the entire left side of the body. During life the left leg was bent over the right at about the level of the knee. The left foot and toes were markedly extended and permanently fixed. The right leg curved toward the median line. Walking must have been difficult, if not almost impossible, as even the pelvic and body axes were obliquely alined. The left half of the face was askew. A more or less constant rheumatic type of pain must have played no small part in his existence. Yet with this man there were found many distinctive artefacts, such as bear's teeth, bone needles, a shell necklace, discoidals and an effigy pipe. All these factors indicate that he probably held some important position among his fellows, and it becomes more significant when one considers the paucity of material expression associated with other burials in the same mound.[1] He may even have been the traditional "medicine man."

The exact chronological position of this skeleton is necessarily a matter of estimation. The mound in which it was found belongs to the last of the three bluff cultures, which precedes the Columbian era by several centuries, and is subsequent to the Hopewell culture (about 2,000 years old). Thus, its age may safely be approximated at 1,000 years.

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1. The apotheosis of cripples is by no means a new idea. Well known examples of this are the deification of achondroplastic dwarfs by the Egyptians as described by: Ruffer, Sir M. Armand: Studies in the Paleopathology of Egypt, ed. by R. L. Moodie, Chicago, University of Chicago Press, 1921, pp. 35-49. Dawson, W. R.: Dwarfs and Hunchbacks in Ancient Egypt, Ann. M. Hist. **9**:315, 1927.

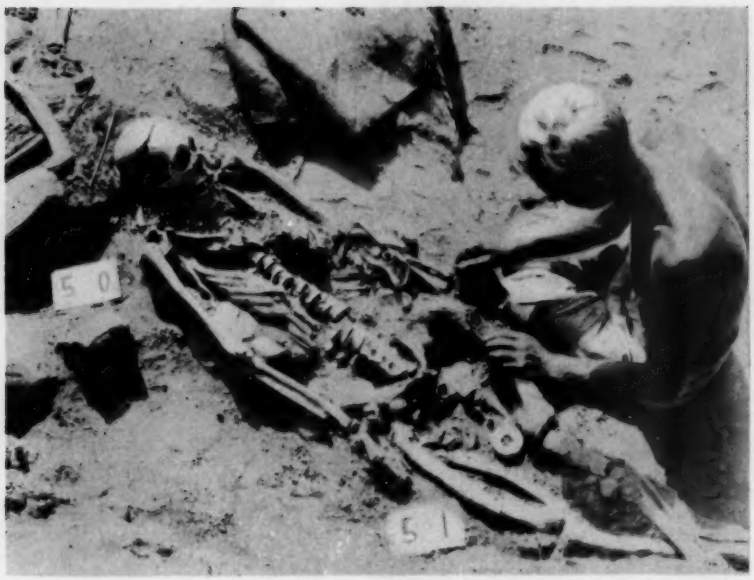

Fig. 1.—View in situ of skeleton (F 14-50) showing osteitis fibrosa, Mr. George Neumann removing the left femur (see fig. 2). The number 51 refers to a skeleton the skull of which lay directly beneath the fragile pelvis of this specimen and was responsible for considerable damage. Note coxa vara position of left leg.

Fig. 2.—Posterior view of the left femur, and posterolateral view of the right.

A study of the skeleton indicates that the man to whom it belonged was afflicted with osteitis fibrosa, as evidenced by the following observations: [2]

The left femur presents the most striking pathologic changes in the upper third of the bone. These changes consist of a marked medial bending and an extensive enlargement and overgrowth of bone, with evidence of cavity formation. The bending of the head and neck of the femur on its shaft is such that the axes of these form an angle of approximately 45 degrees downward, and is probably not due to previous fracture. This must have required the man to hold the leg in a marked position of coxa vara, crossing in front of the right leg at about the level of the knee. The enlarged portion of the femur begins slightly above the junction of the upper and middle third of the shaft. Here there is a bony overhanging crest. The anterior surface of this swelling is relatively smooth and presents few perforations or porosities. Those present are mainly at either end of the enlargement. The perforations appearing on the lateral surface seem to have been made during the work of excavation. Bony trabeculations and perforations make up the posterior surface of this region of the femur, and in the upper part bony cords radiate from the margin of the femoral head to the trochanter. The lower portion of the posterior surface presents many projecting osteophytic growths.

The interior of the enlarged portion forms a cyst or large cavity. In its upper portion the cavity is filled with soft, fine, irregular, spongelike bone, derived from the pathologic changes in the bone marrow. The cortical bone about these cavities is very fragile and in places exceedingly thin. A lacelike trabeculation associated with spongy bone is found to extend through the entire marrow cavity on the lateral side. Just above the lateral condyle on the popliteal surface is an eroded, perforated, ulcer-like area, connecting with the peculiar bone formation described in the marrow cavity. This appears to be an early stage in the peripheral invasion of the disease.

In the right femur the pathologic changes are found in the proximal fourth of the bone, and are by no means so extensive. The normal contours are increased in size, with a nodular enlargement above the intertrochanteric crest. The surface here is perforated by hiati, from

2. As here considered, osteitis fibrosa is a primary disease, in contrast with the secondary fibrous osteitis often definitely associated with inflammatory lesions. Primary osteitis fibrosa "is a distinct clinical entity, is very liable to be confounded with osteomalacia, osteitis deformans, or with central bone tumors, and is very puzzling to the practitioner," according to R. L. Knaggs (The Inflammatory and Toxic Diseases of Bone, New York, William Wood & Company, 1926, p. 1246), and I may add that our position as paleopathologists, diagnosing only from the osseous remains, is at times no less dilemmatic.

4 to 8 mm. in diameter, leading into a cavity, continuous with that of the bone marrow. Spongy bone is also found in this cavity. In the unaffected portions the cortex of both femurs is of normal thickness.

The right tibia exhibits a diffuse nodular swelling slightly above the middle of the shaft. On the medial surface there are two deeply eroded areas in the cortex, the smaller of which (2 by 4 cm.) is surrounded by a slightly raised, eburnated ring of bone. Its base is composed of soft spongy bone and irregular bony trabeculae around numerous hiati which lead into the marrow cavity. The larger eroded area (3 by 7 cm.) is similar in appearance, except that the margin is eburnated only in the back and here blends with a diffuse nodulation on the posterior surface. The left tibia was badly broken in situ by roots, and only the lower third of the shaft shows nodular enlargements.

The fibulae of both the right and the left legs present all the pathologic changes described. There are nodules associated with eroded

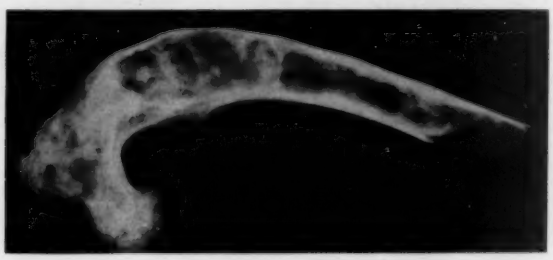

Fig. 3.—Roentgenogram of the left femur showing cyst formation, thinning of cortical bone, trabeculation and abnormal deposition of bone.

areas, and cavities indicative of either cysts or fibrous areas, in various portions of the shaft. Such regions contain spongy bone and trabeculae and have a rarefied cortex. It may be noted here that in the long bones none of the articular surfaces are involved.

The bones of the right foot appear to be unaffected, while those of the left foot show a general increase in porosity of surface. Only the first and second metatarsals of the left foot show any significant pathologic changes. The first metatarsal contains spongy bone throughout and an eroded perforation on the distal end of the dorsal surface. The second metatarsal shows only an eroded area at the proximal end. As the bones of the left foot were uncovered in situ, they delineated the position of a marked talipes equinus.

In the right os coxæ only the ischiopubic ramus and ischial tuberosity are involved by a single cystic swelling extending from the center of the tuberosity into the ramus. The erosion of the surface in this region extends upward to the posterior surface of the acetabular portion

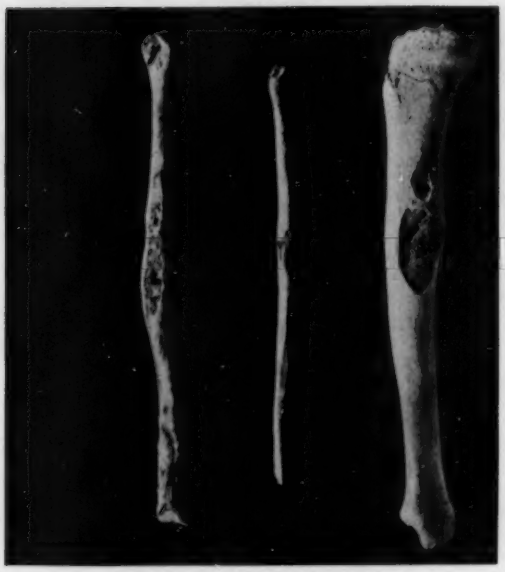

Fig. 4.—Medial views of right and left fibulae and of right tibia.

Fig. 5.—Lateral aspect of left os coxae and posterior view of sacrum. The loss of osseous material in the lower portion of the ileum and that in the right side of the sacrum are due to crushing in the grave, and do not represent a pathologic condition. However, the extensive involvement of the bones is evident. The first coccygeal segment has ankylosed with the sacrum.

of the ilium. A small osteophyte is present at the attachment of the transverse ligament to the acetabular margin. The left os coxæ had been crushed in the grave, but sufficient material remains to show the extensive pathologic changes that had taken place. The portion of the ilium above the acetabulum is ballooned out with a series of cavities to a width of 6.5 cm. The lateral and medial surfaces are much eroded, and many of the hiati show eburnated margins. The interiors of the cavities contain trabeculations and spongy bone. The sacral articular surface is missing.

Sacral involvement is primarily on the left side, as in the pelvis. The enlargement is directed laterally, so that the anterior sacral foramina become ellipses. These open into a large cavity between the first and fifth sacral vertebrae, continuous with the posterior foraminae and with the sacral canal. The articular surface of the left side is much eroded, jagged and perforated, indicating that this joint formed no barrier to the extension of the disease process. A bending of the lower portion of the sacrum to the right may be due to long continued pathologic action.

Extensive changes are to be found in some of the ribs. The first left rib is about three times the size of its opposite in width and breadth, but its length is not increased. Its surface is somewhat eroded at the head, and the body is a mere cavity with thin cortical bony walls. The second, third, fourth and tenth ribs are unaffected. Of the remaining ribs of the left side it was possible to save only the seventh, ninth and eleventh. These are merely fragile laceworks of bone, with only the heads retaining their identity. As their condition is ineffable, one must rely on the accompanying illustrations. On the right side the ribs are unaffected, except for a small portion on the anterior surface at the angle of the fifth.

In the vertebrae the pathologic changes are similar to those described in the other bones. The seventh cervical vertebra has cavitous transverse processes and spine, with characteristic erosion and perforations of the surface. Like changes are also found on the left transverse processes of the fifth to the tenth thoracic vertebrae, and the ninth, tenth and eleventh show involvement of the right transverse processes. The body of the eighth thoracic and that of the second lumbar vertebrae have been perforated by the pathologic process. An incipient perforation is seen in the body of the sixth thoracic vertebra.

The involvement of the skull by the disease is limited to contiguous portions of the left maxilla, palatine bone and pterygoid process of the sphenoid. The anterior portion of the palate is also affected, causing a dissymmetry of the nasal aperture on the left side. The palate here is 1.5 cm. thick, but is of normal size posteriorly. It bulges some-

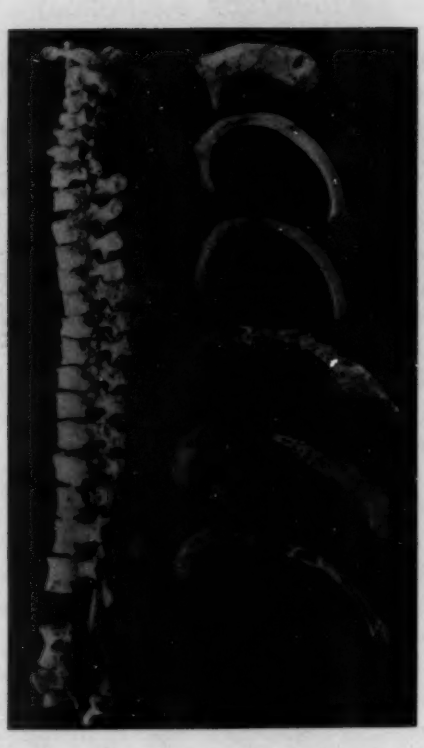

Fig. 6.—Vertebral column viewed from the left side; the third lumbar vertebra was broken, a space representing its location. At the right are the first, second, third, seventh, ninth and eleventh ribs of the left side, of which the second and third are normal.

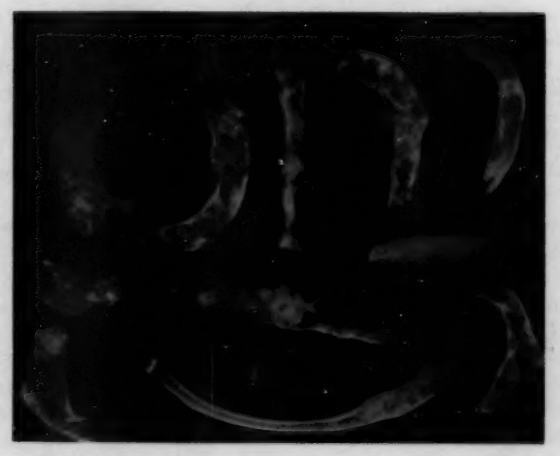

Fig. 7.—Roentgenogram of ribs, showing extensive cyst formation and rarefaction.

what below the normal palatal plate and presents an eroded surface. The pterygoid region on the left side is composed of a hard, porous enlargement of bone with only narrow ridges suggesting the pterygoid laminae. The base of the normal right pterygoid process measures 1.2 cm. across, while the base of the affected side measures 2.5 cm., the pterygoid fossa being essentially eliminated. The palatine canal and other foraminae in this region are patent.

The foregoing material appears to me to indicate clearly that here for the first time is a case of osteitis fibrosa in a prehistoric American skeleton. Osteitis deformans has been encountered, but differs from osteitis fibrosa in important features, both in its effect on the living person and in the condition of the bones after death.[3]

Osteitis fibrosa is a multiple disease of bone characterized by resorption of bone and its replacement by a fibrous connective tissue, associated with formation of cysts. The disease very seldom appears after the age of 40 and may occur before puberty. In recent years many cases have been found in association with parathyroid adenoma. The pathologic changes in the bones show: (1) extensive resorption of bone, which I have termed, macroscopically, erosion; (2) irregular, malformed deposition of bone throughout the fibrous growth;[4] (3) formation of cavities associated with swelling beyond the normal contours of the bone; (4) rarefaction of cortical bone in the involved regions only, the cortical bone elsewhere being of normal thickness and consistency, and (5) a characteristic nodular appearance, as the disease possesses no uniformity of distribution or progress.

Roentgenograms of the entire skeleton have been made, and those of the bones described in detail substantiate the pathologic changes enumerated in foregoing paragraphs.[5] The left femur and ribs present the most characteristic features of the disease (see figs. 3 and 7).

3. There is a recent tendency to consider osteitis fibrosa, osteitis deformans and osteomalacia as a clinical group under the term of osteodystrophia fibrosa. However, from a paleopathologic point of view it seems advisable to retain them as entities so that any remains of a doubtful pathologic nature may be more critically approached, and thus rescued from the oblivion imposed by an all inclusive term.

4. It is understood that the replacement of bone by fibrous tissue can be seen only in fresh specimens, and it is during this active stage of the disease when fibrous tissue predominates, that the bending occurs.

5. Some of the bones that appear normal grossly show in the roentgenograms small areas of rarefaction, which may indicate an incipient process of the disease, but which are indistinguishable from the condition known as spotted atrophy. Such areas are found in the right calcaneus, the right and left astragalus, several of the ribs on the right side and the bodies of the sixth, eighth and ninth thoracic and the second lumbar vertebrae. The acetabula, the heads of the femurs and a few of the vertebral bodies show minute osteo-arthritic changes which are negligible.

Involvement of the skull in the specimen is limited to the left side of the base as described, the roentgenograms showing nothing typical of the condition, the calvarium being normal in thickness and exhibiting no rarefaction.

Osteitis deformans, on the other hand, differs in the following characteristics: 1. As the bone marrow is transformed into fibrous tissue and ultimately into bone, it encroaches on the inner surface of the cortex increasing its thickness. 2. A similar change takes place on the outside through the subperiosteal deposition of layers of bone. Thus in osteitis deformans the cortex may become 1 cm. or more in thickness, which characteristically is uniform throughout the length of the bone, and is seldom associated with the formation of cysts. In typical cases the thickness of the calvarium is increased four or more times the normal. Further, osteitis deformans is a disease of middle age, rarely beginning before the age of 40. These characteristics obviously do not obtain in the specimen described.

It is noteworthy that this case may be classed among the rarities because the involvement is so extensive, although practically unilateral.[6]

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6. Since the foregoing observations were submitted for publication two prehistoric skeletons showing pathologic changes have been reported, for which the diagnosis of osteitis fibrosa has been suggested. The first, showing a bilateral involvement of the humeri only, was described by Leon Pales in his recent book, "Paleopathologie et pathologie comparative," published in Paris by Masson & Cie, 1930. The second is reported by E. A. Hooton, as follows: "Catalogue no. 60061, sex doubtful, aged 35-39: Diagnosis, (1) Spondylitis deformans; (2) Periostitis of mid shaft of left tibia. H. U. Williams, 'probably osteitis fibrosa,'" The Indians of the Pecos Pueblo: A Study of Their Skeletal Remains, New Haven, Yale University Press, 1930.

Notes and News

University News, Appointments, Promotion, Resignations, etc.—Simon Flexner, director of the Rockefeller Institute for Medical Research, has been elected a corresponding member of the French Academy of Sciences in the section of medicine and surgery.

James Lorraine Smith, professor of pathology and dean of the faculty of medicine at the University of Edinburgh, died on April 18, 1931.

The order of the White Lion has been conferred on Frederick G. Novy, professor of bacteriology in the University of Michigan, by the president of the Republic of Czechoslovakia.

James R. Cash, professor of pathology in Peiping Union Medical College, has been appointed professor and head of the department of pathology in the school of medicine of the University of Virginia.

Richard V. Lamar, professor of pathology and bacteriology in the school of medicine of the University of Georgia, has resigned to accept the position of pathologist in the state hospital at Nulledgeville.

It is reported John A. Kolmer has been appointed professor of immunology and chemotherapy in the Temple University school of medicine, Philadelphia.

Israel Davidsohn, formerly pathologist to the Mount Sinai Hospital in Philadelphia, has assumed the duties of pathologist to the Mount Sinai Hospital in Chicago.

Society News.—At its recent meeting the American Association for Cancer Research elected Francis Carter Wood president, Edward B. Krumbhaar vice-president and William H. Woglom secretary and treasurer.

The following are the officers of the American Society of Experimental Pathology for the year 1931-1932: president, Samuel R. Haythorn; vice-president, Peyton Rous; secretary-treasurer, C. Phillip Miller, Jr.; councillors, Carl V. Weller and S. Bert Wolbach.

At the annual meeting of the American Association of Pathologists and Bacteriologists in Cleveland, Ward J. MacNeal was elected president, E. T. Bell vice-president, G. B. Mallory treasurer, Howard T. Karsner secretary and O. T. Avery councillor. The next annual meeting of this society will be held in Philadelphia on March 24 and 25, 1932.

Deaths.—Aldred Scott Warthin, Professor of Pathology in the University of Michigan since 1903, died on May 23, at the age of 65 years.

Abstracts from Current Literature

Experimental Pathology and Pathologic Physiology

JAUNDICE IN EXPERIMENTAL COCCIDIOSIS OF RABBITS. GEORGE W. BACHMAN and PARIS E. MENENDEZ, Am. J. Hyg. **12**:650, 1930.

Tests on 31 rabbits infected with *Eimeria stiedae* gave 111 positive reactions for bilirubin, of which 90.1 per cent were direct, 8.1 per cent indirect and 1.8 per cent were biphasic. One rabbit slightly infected failed to give a positive reaction. The large variations in quantitative estimates of bilirubin contents in these rabbits are probably due in part to the fact that the determinations were made at intervals of days and not at intervals of hours and also to the amount of epithelial destruction of the bile ducts during the various stages of schizogony. No attempt was made to explain the indirect and biphasic reactions obtained in these tests. The intensity of the infection found in some of these rabbits could have caused the rupture of small blood vessels and the destruction of hepatic cells, which would be sufficient to account for the small percentage of hemolytic jaundice. The high percentage of direct immediate reactions obtained in these tests indicates obstructive jaundice. Microscopic studies of stained sections of livers in the early stages of schizogony show the epithelial cells of biliary passages parasitized and swollen. In the latter stages of the infection the biliary passages may be seen plugged with proliferated cells of the epithelium and oocysts. In heavy infections the gall ducts and gallbladder are plugged with the numerous orange-yellow colored oocysts. The compaction of these oocysts gives rise to obstructive jaundice.

AUTHORS' SUMMARY.

EDEMA. HERMAN ELWYN, Am. J. M. Sc. **180**:781, 1930.

We have thus come to the understanding that in every case of general edema there is a slowing up in the rate of movement of water from the depots through the tissue barriers to the blood stream. With the normal intake of water and salt and their rapid removal from the blood into the tissues, the free water there is rapidly increased. When a certain amount of water has accumulated, it becomes visible as edema. The slowing is the result of a central regulatory change and affects the constellation of electrolytes in the tissue barriers through which the water moves to the blood and lymph streams. This slowing is produced, first, whenever the water content of the blood threatens to be unduly increased, as in cardiac failure, or in acute diffuse nephritis; second, when the change is primarily in the regulatory center, along with the depression of other vegetative functions, especially of the basal metabolic rate. This is the case in chronic undernutrition and in chronic wasting disease. Third, it is produced when there is a primary disturbance in the central regulation for the control of sodium chloride in the body. This is so in certain cases of edema without cardiac or renal diseases, and without chronic undernutrition.

AUTHOR'S SUMMARY.

OVARIAN AND PITUITARY CHANGES ASSOCIATED WITH HYDATIDIFORM MOLE AND CHORIO-EPITHELIOMA. E. NOVAK and A. K. KOFF, Am. J. Obst. & Gynec. **20**:481, 1930.

According to certain observers, multiple lutein cysts of the ovaries occur in association with hydatidiform mole in 60 per cent of cases and with chorio-epithelioma in about 10 per cent. Most of the statements are based on the results of abdominal

palpation. Such cysts disappear spontaneously after evacuation of the uterus. The authors had occasion to examine the uterine contents and ovaries of four women, two of whom had a hydatidiform mole; the other two a chorio-epithelioma. The pituitary gland of one of the latter was also available for study. The ovaries of all the women contained cysts—the "hyperreactio luteinalis polycystica." In the pituitary, only the usual changes accompanying pregnancy existed, but these had persisted longer than usual. To explain the conditions the following interreactions are assumed: The trophoblastic increase in chorio-epithelioma (persisting in the metastases after evacuation of the uterus) is responsible for the pituitary reaction. The anterior lobe of the pituitary, "the motor of the ovary" in its normal cyclical activity also causes the ovarian changes of normal pregnancy and also those occurring in hydatidiform mole and chorio-epithelioma.

GEORGE RUKSTINAT.

A COMPARISON BETWEEN SIMULTANEOUS EQUAL-SIZED, CLOSED OBSTRUCTION OF THE DUODENUM AND ILEUM. J. J. MORTON and W. C. SULLIVAN, Arch. Surg. **21**:531, 1930.

The distal 10 cm. of the ileum and of the duodenum were obstructed in dogs. Every twenty-four hours the loops were aspirated, and the contents measured and reinjected in order to estimate accurately the rate of secretion without disturbing the intra-intestinal pressure relations which had occurred. The secretory rate for the ileum is practically negligible as compared with that of the duodenum, which is rapid. The intra-enteric pressure is from four to seven times higher in twenty-four hours in the duodenum than in the ileum. The distensibility of both loops is about the same, but the ileum increases in length as compared with the obstructed loop of the duodenum. In those cases in which spontaneous rupture occurred in the closed loops, the closed duodenal loop was the one affected. Death in these animals was due to peritonitis. In the other animals, death was due to toxemia, and after death it was noted that a pressure equal to 1,600 mm. of mercury was necessary to rupture the closed loops. However, as rigor mortis advances, the pressure required to produce rupture is lower. This is due to the loss of elasticity of the musculature.

N. ENZER.

THE EFFECT OF PERICARDIOSTOMY ON THE MECHANICS OF THE CIRCULATION. C. S. BECK and W. V. COX, Arch. Surg. **21**:1023, 1930.

Experiments were made on dogs to determine the influence of atmospheric pressure on the action of the heart after pericardiostomy. A preliminary operation is necessary in dogs, because there is no triangle of safety in the precordial zone. Hence, the pericardium must be sutured to the left thoracic wall over an area about 3 cm. in diameter. Pericardiostomy may be performed about seven weeks later, and arterial and venous pressure and cardiac output determined. Following pericardiostomy, there is a sustained rise in venous pressure and a fall in the arterial pressure of from 8 to 30 mm. of mercury. Atmospheric pressure acts as an air tamponade on the heart and the great vessels within the pericardial sac, and produces dilatation of the sac. Hence, operative procedures can hold out reasonable hope for success only in cases with adequate circulation.

N. ENZER.

A NEW TRANSMISSIBLE STRAIN OF THE LEUCOSIS (LEUCEMIA) OF FOWLS. J. FURTH, J. Exper. Med. **53**:243, 1931.

Myeloid leukosis and erythroleukosis can be transmitted from one bird to others by emulsions of infiltrated organs, whole blood cells and plasma. Inoculation is more often successful with blood cells or with whole blood than with plasma or with emulsions of organs infiltrated as the result of leukosis. Inoculation with material from a bird with myeloid leukosis or with erythroleukosis produces both conditions and in many instances mixed forms with characteristics of both. Evi-

dence is wanting that lymphoid leukosis is caused by the agent that transmits myeloid leukosis and erythroleukosis. The occurrence of lymphoid leukosis among the birds inoculated with material from myeloid leukosis or erythroleukosis may be explained as spontaneous disease. Injury to cellular structure by treatment with distilled water or by repeated freezing and thawing does not destroy the agent that transmits the disease. Berkefeld filtrates have failed to transmit regularly myeloid leukoses or erythroleukosis. The evidence obtained shows, however, that the transmissible agent is filterable, although there are technical difficulties in its filtration.

AUTHOR'S SUMMARY.

TRANSMISSION EXPERIMENTS WITH LEUCOSIS OF FOWLS. E. L. STUBBS and J. FURTH, J. Exper. Med. **53**:269, 1931.

It is shown, in a carefully controlled experiment, that the leukemia of fowls can be readily transmitted from chicken to chicken by injection. Of twenty-five fowls, thirteen were given intravenous injections of blood from a chicken with erythroleukosis and twelve injections of blood from a chicken with myeloid leukosis. The birds that received the injections and an equal number of controls that did not were kept in tiers of alternating cages under as nearly identical conditions as possible. The donors, the controls and the birds that were given injections were all of the same stock and of the same age. In the two series, thirteen or 52 per cent of the twenty-five fowls that were inoculated developed leukemia within from four to ten weeks after injection. The two types of leukemia, erythroleukosis and myeloid leukosis, developed in both groups irrespective of the type used for injection. Among controls that were not given injections, erythroleukosis or myeloid leukosis were not observed. Lymphoid leukosis occurred in one fowl that had received an injection but since it also occurred in one control it may be assumed that it was probably not caused by the material used for injection.

AUTHORS' SUMMARY.

A CRITERION OF HEMORRHAGIC DIATHESIS IN EXPERIMENTAL SCURVY. G. DALLDORF, J. Exper. Med. **53**:289, 1931.

The degree of scorbutic change in the vessels of animals with experimental scurvy can be roughly measured by establishing the amount of negative pressure required to produce petechial hemorrhages in the skin. The test shows that the hemorrhagic diathesis in experimental scurvy develops earlier than any other known sign of the disease and that it persists in some degree throughout. The response of the blood vessels to the administration of antiscorbutic substances is extremely rapid as shown by the test, but it varies with the amount of antiscorbutic substance given and its method of administration. The changes in the resistance of the vessels follows a curve which rises toward recovery during the end of the first week that a scorbutic diet is fed, reaches a peak in the second week, and then falls steadily during the remainder of the course of the disease. This indicates that the course of the disease is not constant and progressive. The test may have clinical value in the diagnosis of scurvy.

AUTHOR'S SUMMARY.

EXPERIMENTAL DUST INHALATION IN GUINEA PIGS. F. HAYNES, J. Hyg. **31**:96, 1931.

All inhaled particles are rapidly ingested by certain individual cells belonging to the alveolar epithelium. These cells (dust cells or phagocytes) remain in the parenchyma of the lung until they have ingested an amount of dust constituting the cell's saturation load. This load varies with different dusts. A cell that has attained its saturation load sooner or later becomes detached from the alveolar wall and either migrates into the lymphatics or becomes free in the alveolus. In the former case, it passes into the pulmonary lymphoid tissue and thence to the

bronchial lymph glands. In the latter case, it passes up the bronchial tree to be either coughed out or swallowed. Dust cells that speedily leave the alveolar wall are principally eliminated by the bronchi. In the case of a dust cell being eliminated from the lung via the lymphatics, it may be arrested in the periatrial lymphatics on account of its bulk. The dam thus produced offers obstruction to the passage of other dust cells shed into the alveoli. Groups of free dust cells in the obstructed alveoli form plaques, which degenerate and liberate their dust. This is again ingested, and the irritation caused by such a process may lead to fibrosis. The continued presence of dust-laden cells in the lymphatics may set up a foreign body irritation, with resulting fibrosis. Most inhaled particles contain soluble matter, at least to a very small extent. The solute may be either harmlessly active or toxic. If the former, the cell is stimulated to detach itself from the alveolar wall, and so remove the dust. If the latter, the solute effects the viability of the phagocyte, which becomes less able to detach itself. At the same time the solute diffuses into the adjacent tissues, with irritation to them, and consequent fibrosis. The more soluble form of a substance causes greater pulmonary damage than the less soluble. The solute, therefore, plays a large part in the determination of damage.

While many dusts cause pulmonary fibrosis, silica is the dust par excellence predisposing to tuberculosis. This is doubtless due to its influence in forming a medium suitable not only for the survival but the proliferation of the tubercle bacillus in the lung (Kettle, private communication). The harmful effects of soluble silica may be neutralized by simultaneous administration of basic dusts such as aluminum hydroxide or magnesium carbonate, though the latter are themselves harmful when inhaled alone. It is suggested that their respective solutes combine to form monosilicate. Monosilicates do not appear to have any harmful effect on the lung. Heavy inhalations of any dust are liable to cause pulmonary damage. The intensity of the initial pulmonary reaction to a dust is very generally in inverse ratio to the degree of eventual damage caused by the dust.

AUTHOR'S SUMMARY.

THE EFFECTS OF INHALATION OF BENZINE AND BENZENE. M. SCHMIDTMANN, Klin. Wchnschr. **9**:2106, 1930.

The inhalation of small quantities of benzine and benzene over long periods gave rise in animals to chronic bronchitis, emphysema, epithelial proliferation in bronchi and alveoli and atelectasis, but carcinoma did not develop. The anemia and other blood changes characteristic of benzene poisoning gradually appeared.

GOUT IN AN INFANT FIVE WEEKS OF AGE. E. MAYER v. SCHOPF, Klin. Wchnschr. **9**:2148, 1930.

The author reports the details of the clinical course and examinations of the tissue in a case of gout in a child 5 weeks old. The urates were formed from endogenous purines. The kidneys were contracted.

EDWIN F. HIRSCH.

HYPERINSULINISM WITH HYPOGLYCEMIC SYMPTOMS. F. KRAUSE, Klin. Wchnschr. **9**:2346, 1930.

A disease was observed in a man, aged 43, which was caused by hypoglycemia, and which is interpreted as a hypoglycemic reaction of the organism. This condition of spontaneous hypoglycemia is caused by hypersecretion of insulin, and the morphologic basis is probably a tumor of the pancreas.

AUTHOR'S SUMMARY.

CIRCULATORY AND TUBULAR INSUFFICIENCIES OF THE KIDNEY. ERWIN BECHER, Klin. Wchnschr. **9**:2350, 1930.

Circulatory and tubular insufficiencies of the kidney are distinguishable. In the circulatory insufficiency which occurs with acute nephritis and cardiac insuffi-

ciency, the total nonprotein nitrogen of the blood, the urea and the uric acid are increased, and other changes are absent. This is due to the decreased circulation of the blood through the kidney and without, or only slightly, altered tubular function. With true tubular insufficiency, there is a marked increase of the putrefactive substances of the blood as well as of the nitrogenous substances. There are a hyposthenuria or isosthenuria and light-colored urine, because the oxidation of the urochrome in the kidney does not occur.

AUTHOR'S SUMMARY.

BLOOD DEPRESSOR SUBSTANCE IN TISSUES. FRITZ LANGE, München. med. Wchnschr. **77**:2095, 1930.

A thermostabile substance with depressor properties has been extracted from many different visceral tissues, and by exclusion is thought to be held in the peripheral portions of small blood vessels. Renal tissues contain an appreciable amount of this substance. The ingestion of renal tissue has been found in cats and man to lower the blood pressure. Preliminary tests indicate that the active substance is not purine, choline or histamine.

EDWIN F. HIRSCH.

THE INFLUENCE OF THE SYMPATHETIC NERVOUS SYSTEM ON THE PANCREAS. BORIS GOLDSTEIN, Ztschr. f. d. ges. exper. Med. **74**:128, 1930.

Experiments on the isolated pancreas indicate that the effect of the sympathetic nervous system on the secretory activity of the pancreas is exerted in two ways: it strengthens the ferment-forming processes and its helps to retain the ferments in the cells (apparently by affecting the cellular permeability).

PEARL ZEEK.

Pathologic Anatomy

STRUCTURAL CHANGES IN YELLOW FEVER. O. KLOTZ and T. H. BELT, Am. J. Path. **6**:655, 663 and 689, 1930.

In yellow fever, the spleen, like the liver, presents no distinctive gross features comparable with those seen under the microscope. Active hyperemia is met with in about 80 per cent of cases, but is unaccompanied by leukocytic infiltration. There is absence of hyperplasia in the fixed tissues of the pulp. Changes in the malpighian corpuscles characterize the splenic picture. Here we recognize four phases of the reaction:

1. Mononucleosis. The type cell is an undifferentiated mononuclear derived from the reticular tissue of the follicle; it never entirely disappears during the entire course of the disease.

2. Lymphopenia. There is a striking loss of lymphocytes from the whole organ, which persists throughout the reaction.

3. Hyperplasia of the fixed tissues of the follicle. False germinal centers are formed.

4. Degeneration. This is manifested throughout the whole spleen by vesicular nuclei and waxy degeneration of cytoplasm. False germinal centers undergo retrograde changes, amounting sometimes to actual necrosis. Pseudomitosis of the primitive mononuclears is observed. Large fragmented nuclear forms appear in the pulp.

A third of the cases show a few large multinucleate giant cells resembling megakaryocytes. A moderate eosinophilia is commonly observed in the later stages of the reaction. Changes in lymph glands parallel those in the splenic corpuscles, which is evidence of the fact that the toxin of yellow fever has a selective action on lymphopoietic tissue. We have found a careful examination of the spleen to be

frequently helpful in facilitating a pathologic diagnosis when yellow fever must be differentiated from other conditions giving rise to lesions in the liver and kidneys.

Grossly, the liver in yellow fever is characterized by the absence of distinctive changes such as are seen under the microscope. Microscopically, the hepatic tissue presents noninflammatory necrosis and necrobiosis of the parenchyma, unaccompanied by collapse of the tissue or interstitial hemorrhage. The outstanding change is a coagulative hyaline necrosis (the Councilman lesion), which does not attack the hepatic cells in an orderly fashion, but occurs as a diffusely sprinkled lesion often most marked in the midzone (the da Rocha Lima distribution). This specific necrosis is always preceded or accompanied by fatty degeneration and cloudy swelling. In the earliest stages it is characterized by the formation of dense acidophil masses within the neutrophil cytoplasm of the hepatic cells. Later, discrete, highly refractile, hyaline globular bodies appear, often possessing a flattened, pyknotic nucleus at the periphery of the mass. These bodies are usually honeycombed with fat vacuoles which they have incorporated. The process goes on to massive involvement of parenchymal tissue and ends in cellular disintegration, but no appreciable autolysis of the affected cell structures is seen in the acute stages. The Kupffer cells suffer some damage, but not necrosis. The vascular system, biliary channels and stroma are uninvolved in the disease. Specific nuclear inclusions were found in the livers of seventeen of nineteen monkeys of the species *Macacus rhesus,* and in those of twenty-three of ninety-three human beings with yellow fever. Their identification was attended with difficulties, but when their presence could be established the diagnosis was thereby facilitated. The store of glycogen in the liver is depleted in proportion to the severity of the lesion. The lesions of the liver in yellow fever possess several features in common with the lesions of the liver in other diseases due to virus.

Six *rhesus* monkeys which had recovered from experimental yellow fever showed complete and scarless regeneration of the liver and kidney. This bears out clinical evidence that neither cirrhosis of the liver nor contracted kidney follows yellow fever in man. Special attention is directed to the sequence of events taking place in the liver. Except in cases of chloroform poisoning, hepatic damage of equal magnitude rarely occurs without producing some scar formation. The liver in yellow fever proves that destruction of parenchymal cells alone is not a sufficient stimulus to induce replacement fibrosis. The absence of fibrosis in the liver and kidney is due to a peculiar immunity which the stromal structures manifest toward yellow fever; there is no stimulation of connective tissue elements during the acute stage of the disease. The reasons for this are, we believe, related to the noninflammatory, nonautolytic character of the acute pathologic process and to the absence of thrombosis in the small parenchymal blood vessels. Regeneration originates in islands of parenchymal cells that have survived the attack, and quickly restores the tissues to their original state.

AUTHORS' SUMMARIES.

ENDOCARDIAL POCKETS. OTTO SAPHIR, Am. J. Path. **6**:733, 1930.

In two cases of subacute bacterial endocarditis of the aortic and mitral valves with insufficiency of the aortic valve, endocardial pockets with openings toward the aorta were found on the interventricular septum of the left ventricle. The initial lesion which brought about the formation of the pockets was a circumscribed parietal endocarditis. The continuous regurgitation formed the pockets secondarily. In one case of rheumatic endocarditis of the mitral valve with insufficiency of this valve, endocardial pockets were present in the left auricle. These pockets were open toward the mitral valve. They also were inflammatory in origin and were formed secondarily by the regurgitation after the insufficiency of the mitral valve had been established. In two cases of syphilitic involvement of the aortic valve with insufficiency of this valve, endocardial pockets opening toward the aorta were found. These pockets were caused primarily by the mechanical irritation of the regurgitating blood columns. Two cases of syphilitic involvement of the aortic valve with insufficiency of this valve and marked stenosis

of the conus arteriosus sinister, and one case of rheumatic endocarditis of the aortic valve with stenosis of its orifice, showed endocardial pockets on the interventricular surface of the left ventricle. These pockets were open toward the apex of the heart. They were brought about by the mechanical irritation of the systolic blood stream acting as a trauma on the endocardium in the region of the stenosed portions. Diastolic endocardial pockets are evidence in favor of the view of actual regurgitation of blood volume. The nomenclature of "diastolic pockets," referring to those open toward the aorta, and "systolic pockets," referring to those open toward the apex (Krasso), is justified. Endocardial pockets cannot be regarded as manifestations of functional adaptation.

AUTHOR'S SUMMARY.

TRANSFORMATION OF SINUSOIDAL ENDOTHELIUM INTO THE ORDINARY CAPILLARY TYPE. F. A. MCJUNKIN, Am. J. Path. **7**:9, 1931.

In granulation tissue within the liver, the capillaries may arise in the usual way by angioblastic proliferation, or sinusoids may persist as capillaries. In both instances the vessels are continuous with the sinusoids in the adjoining lobules. With loss of contact with living hepatic epithelium the endothelium becomes less phagocytic. The peculiarities of sinusoidal endothelium depend on its functional activity, which, in turn, is determined by its normal histologic position. From the behavior of sinusoidal endothelium present in granulation tissue, it appears not to be a distinctive type of cell.

AUTHOR'S SUMMARY.

THE CIRCULATORY PATTERN IN THE ISLANDS OF LANGERHANS. J. S. P. BECK and B. N. BERG, Am. J. Path. **7**:31, 1931.

An anatomic study of the circulatory pattern in the islands of Langerhans was made. The arrangement corresponded with observations made in vivo. The importance of the anatomic arrangement of the blood supply in preserving the islands in the presence of circulatory disturbances in the pancreas is discussed.

AUTHORS' SUMMARY.

INTERACINAR EPITHELIUM OF THE THYROID GLAND. A. R. MORITZ, Am. J. Path. **7**:37, 1931.

This study indicates that in normal thyroid glands of fetuses, children and adults, in pathologic glands the seat of hypertrophy and hyperplasia, in nodular goiter and in adenomas of the thyroid gland, the mechanics of hyperplasia are essentially similar. New follicles are formed by intrafollicular and extrafollicular proliferation of epithelium, and the secondary follicles may lose their parent connection and become isolated units. In the scattered foci of hyperplasia in normal thyroid glands, as well as in the glands that are the seat of pathologic hypertrophy and hyperplasia, labyrinthine intercommunication of acini exists and is probably limited to the connection of primary with secondary acini. Solid masses of undifferentiated interfollicular epithelium are found in both normal and pathologic glands, but such masses are readily accounted for as detached extrafollicular buds. Evidence contrary to certain observations by Rienhoff concerning the mechanics of hyperplasia in the thyroid gland is presented.

AUTHOR'S SUMMARY.

EXPERIMENTAL GLOMERULONEPHRITIS IN A MONKEY. E. T. BELL and B. J. CLAWSON, Am. J. Path. **7**:57, 1931.

A form of chronic diffuse glomerulonephritis was produced in a monkey by repeated intravenous injections of streptococci over a period of four years. The lesion was characterized histologically by marked increase in capillary endothelium and increase in the thickness and number of layers of capillary basement membrane. Histologically, the glomerular lesion resembled human "lipoid nephrosis of mixed type," except that no fat was present.

AUTHORS' SUMMARY.

CHRONIC TYPHOID CHOLECYSTITIS. F. B. MALLORY and G. M. LAWSON, JR., Am. J. Path. **7**:71, 1931.

The gallbladders of seven typhoid carriers are described. A common histologic picture was found (diffuse lymphocytic infiltration of mucosa, with focal accumulations in the form of typical lymph nodules). A review of 400 routine slides of chronic cholecystitis showed a similar lesion in 6.5 per cent of the cases. A review of the clinical histories showed that only 4.9 per cent of the cases with negative histories showed this picture as against 25 per cent of cases with positive histories. It is felt that the lesion described is characteristic of chronic typhoidal cholecystitis, but not pathognomonic of it. It is suggested that it is not specific of any organism, but represents a reaction to persistent infection of the bile in contrast to the more usual type of chronic cholecystitis with sterile bile and persistent infection of the wall.

AUTHORS' SUMMARY.

INFECTIOUS CIRRHOSIS. H. E. MACMAHON, Am. J. Path. **7**:77, 1931.

Uncomplicated infectious cirrhosis is one of the rarer diseases of the liver. It is caused probably in most instances by the colon bacillus, and is characterized by variable proliferation of connective tissue and of bile ducts about the portal areas. Obstructive cirrhosis resulting from prolonged biliary obstruction is a much more common condition, although less conspiculous and hence frequently overlooked. Most cases of infectious cirrhosis are found in combination with obstructive cirrhosis, but even this combined type is relatively rare and is almost invariably fatal.

AUTHOR'S COMMENT.

BIOLOGIC AND HISTOLOGIC STUDY OF LYMPH NODES IN SYPHILIS. E. SALEEBY and S. S. GREENBAUM, J. A. M. A. **96**:98, 1931.

The inguinal lymph glands from twenty-one syphilitic patients were studied histologically and biologically. In five cases we were able to find *Spirochaeta pallida* in the sections, while in others only dark stained granules were observed. Of the animals into which the glands were transplanted, thirteen became infected after the first transplant and three after the second transplant. The organs from nine of the infected rabbits were studied histologically for spirochetes. The testes were infected in all the cases, the lymph glands in five and the heart and the aorta in two. Dark stained granules were present in most of the lymph glands and in the heart. *Spirochaeta pallida* was demonstrated in all sections of the testicles of the animals. In one animal, rabbit 8, we found fragments of the organism in all the sections. The heart showed them in two cases (8 and 3) and the lymph glands in five cases. Of the eight animals in which a second transplant was made, three became infected after eighty-one, seventy-two and sixty-three days. The remaining five became infected following the first transplant. The time varied from twenty-eight to eighty-seven days. Three rabbits became infected after the second transplant, and the remaining five were negative after the first and second transplants. The rabbits receiving injections of the human glands in which spirochetes were demonstrated "came up" in twenty-eight, forty-three, seventy, sixty-five and sixty-eight days. In comparing this series with the other we find little difference in the average number of days.

AUTHORS' SUMMARY.

MILIARY PULMONARY DISEASE OF UNKNOWN NATURE. R. R. SAYERS and F. V. MERIWETHER, Pub. Health Rep. **45**:2994, 1930.

On roentgen examination of miners a number of cases of discrete, shotlike spots in the lungs were noted. Others have referred to such cases as cases of miliary calcification of the lungs. Sayers and Meriwether found aspergilli in the sputum of miners with such miliary nodules in the lungs, and consequently they suggest that the nodules may be due to fungus infections.

ASBESTOSIS BODIES IN THE SPUTUM. F. W. SIMSON and A. S. STRACHAN, J. Path. & Bact. **34**:1, 1931.

The inhalation of asbestos dust in high concentrations leads to the appearance of asbestosis bodies in the sputum in a large percentage of the workers exposed thereto. They were present in forty-eight of fifty workers examined. Asbestosis bodies were as easily demonstrated by direct thick films as by the antiformin method. The sputum was always mucoid when there were no bronchial complications. It may resemble egg albumin. In none of the sputums were tubercle bacilli demonstrated. Study of the intracellular asbestosis bodies in these cases suggests that they are formed by the deposition on the asbestos fiber of an iron-containing substance elaborated by the cell.

AUTHORS' SUMMARY.

EXPERIMENTAL LIVER NECROSIS FROM SHALE OIL. C. J. POLSON, J. Path. & Bact. **34**:5, 1931.

Necrosis of the liver was produced in rabbits and rats by the intraperitoneal administration of shale oil. By graduating the dose it was possible to produce all stages, from acute necrosis to cirrhosis. These lesions formed one continuous series and were almost indistinguishable from those of the "atrophic" series in man. The difficulties arising from the presence of naturally occurring disease were largely overcome by laparotomy and biopsy of the liver. Shale oil is clearly an active poison to the liver. Attention is drawn to the distinct differences between the action of the oil and that of its noncarcinogenic residue.

AUTHOR'S SUMMARY.

MELANOSIS COLI. M. J. STEWART and E. M. HICKMAN, J. Path. & Bact. **34**: 61, 1931.

Melanosis coli is due to the deposition of a melanin-like pigment within large mononuclear cells in the mucous membrane of the gut. It is limited in most cases to the large intestine and appendix, and ranges in intensity from gray or buff through dark gray or brown to inky black. Metastasis of pigment to the submucosa and mesocolic lymph glands may occur in the more advanced cases. The chief causative factor is chronic intestinal stasis, whether resulting from organic obstruction or from simple constipation. The more extreme grades are comparatively rare, but if the slighter forms are included, the incidence is fairly high, 11.2 per cent in an unselected series of 600 autopsies at all ages. In persons over the age of 40 the incidence is higher, 17.7 per cent, and in two series of cases of carcinoma of the colon it was 48.8 per cent and 55 per cent, respectively. In most of these the melanosis was more intense above than below the growth. The most acceptable theory of the mode of formation of the pigment is Pick's—that aromatic products of the disintegration of proteins are absorbed from the colon and converted into melanin within the connective tissue cells by the action of a tryrosinase-like ferment.

AUTHORS' SUMMARY.

COMPENSATORY HYPERTROPHY OF THE ADRENAL CORTEX IN THE RABBIT. E. M. MACKAY and W. S. POLLAND, J. Path. & Bact. **34**:73, 1931.

Removal of one adrenal in the rabbit is followed by compensatory hypertrophy of the remaining one due entirely to an increase in the size of the cortex. This compensatory hypertrophy is less than that following unilateral adrenalectomy in the rat.

AUTHORS' SUMMARY.

MULTIPLE CONGENITAL SUBEPENDYMAL XANTHOMAS. PIETRO REDAELLI, Arch. ital. di anat. e istol. pat. **1**:455, 1930.

The author describes a case of hydrocephalus in a boy, 7 months old, with multiple congenital subependymal nodules in the lateral ventricles, which were

enormously dilated with a clear fluid. The nodules were of pinhead size and were composed of cells that contained refractory neutral fats and also fatty acids.

EMIL WEISS.

CYANOSIS FROM SCLEROSIS OF THE PULMONARY ARTERY. F. SCHIASSI, Arch. di pat. e clin. med. **9**:526, 1930.

The author reports a case of chronic cyanosis due to sclerosis of the pulmonary artery with obliteration of the smaller branches.

E. HAAM.

INFARCTION DUE TO SCLEROSIS OF THE PULMONARY ARTERY AND THROMBOSIS. G. INVERNIZZI, Arch. di pat. e clin. med. **9**:590, 1930.

The author describes infarction of a whole lobe of the lung due to thrombosis in a large branch of the pulmonary artery, which was the seat of a primary sclerosis involving all the branches.

E. HAAM.

CONGENITAL MALDEVELOPMENTS OF THE DIAPHRAGM. W. PUTSCHAR, Beitr. z. path. Anat. u. z. allg. Path. **85**:47, 1930.

Putschar describes thirteen examples of complete defect of the diaphragm and two of diaphragmatic hernia. The two hernias were observed in children, one of the left side in a new-born female infant and a para-esophageal hernia in a child whose age or sex could not be determined from the preparation. Of the diaphragmatic defects, two were noted in adults and eleven in fetuses or infants. In only one case was the defect of the right side; in the remainder, it was of the left side. Only three of the thirteen subjects with defective diaphragms were males; in one of the two adults, the sex could not be determined from the specimen available. Four of seven female fetuses or infants with defects of the left side were anencephalic monsters, and one was a diprosopic monster. Of the three male fetuses or infants with defect of the left side, two were dicephalic. In the defect of the right side, the right lobe of the liver and parts of the large and small intestine were in the thoracic cavity. In the defects of the left side, the spleen, part of the stomach and parts of the large and small intestine were invariably in the thoracic cavity; in some of the cases the pancreas, the left lobe of the liver and the left kidney and suprarenal were also displaced into the thoracic cavity. Putschar discusses the various theories that have been propounded to explain the genesis of maldevelopments of the diaphragm, but believes that exact knowledge is still too incomplete to permit definite conclusions. The frequent association of other developmental anomalies, some of which, as absence of an umbilical artery in three of his cases, must have arisen before the formation of the diaphragm was initiated, incline him to place greater weight on abnormalities of the germ plasm than on purely mechanical factors in the genesis of diaphragmatic maldevelopments.

O. T. SCHULTZ.

EOSINOPHILIA IN MALIGNANT ENDOCARDITIS. W. S. BOIKAN, Folia haemat. **42**: 164, 1930.

There is reported a case of long standing allergic seasonal eczema, complicated by thrombo-endocarditis and showing marked eosinophilia. The postmortem observations were those of intense eosinophil granulopoiesis in the bone marrow and extensive infiltrations of mature eosinophils in the internal organs about embolic foci of necrosis. From the evidence adducted the conclusion is drawn that the eosinophilia of blood and tissue represented the purposeful response of a bone marrow modified by allergy.

AUTHOR'S SUMMARY.

THE RELATIONSHIP BETWEEN THE CLINICAL PICTURE OF GRAVES' DISEASE AND THE HISTOLOGY OF THE THYROID GLAND. E. MAYER and A. C. FÜRSTENHEIM, Virchows Arch. f. path. Anat. **278**:391, 1930.

Forty-seven goiters removed by operation were examined, and the histologic structure was compared with the clinical observations. The macroscopic appearance of the glands, in regard to the diffuse or the nodular form of goiter, is regarded as being without significance. In twenty-three cases the condition was diagnosed clinically as severe Graves' disease; eight patients did not show any thyrotoxic symptoms, and fourteen were treated prior to operation with Lugol's solution.

Polymorphism of the acini, columnar epithelium and thin colloid were, in former years, fairly regular observations in Graves' disease. But since several years—about since the introduction of the preoperative administration of iodine—the most commonly observed change in Graves' disease has been the macrofollicular colloid goiter with some papillary proliferation of the epithelium. The height of the epithelium does not correspond to the grade of thyrotoxic symptoms. In severe Graves' disease the epithelium is occasionally cubical, and the walls of the alveoli are smooth and without papillations. In cases without hyperthyroidism, marked projections of the epithelial wall can be found.

There is a better relationship between the clinical symptoms and the staining quality of the colloid, especially when the methods of Mallory and Kraus are applied. After the administration of iodine, the histologic picture of hyperplastic glands seems changed, not so much in the appearance of the epithelium as in the quality of the colloid. Thyroid glands obtained from patients with exophthalmos did not differ from those from patients without involvement of the eyes.

C. A. HELLWIG.

COMPRESSION OF SPINAL CORD BY ARACHNOID CYSTS. K. NICOLAYSEN and M. HAALAND, Norsk mag. f. laegevidensk. **91**:577, 1930.

In a man, 45 years old, compression of the dorsal part of the spinal cord with resulting paralysis was relieved completely by enucleating four small cysts in the pia-arachnoid. The fluid in the cysts was clear, watery and free from parasitic elements; the walls were thin, fibrous and lined on the inner surface by a single layer of low cells. The nature of the cysts remained obscure.

DISTRIBUTION AND DISAPPEARANCE OF CONGO RED AND GRANULAR STORAGE FACTORS OF THE RETICULO-ENDOTHELIAL CELLS. Y. TAKEDA, Jap. J. Exper. Med. **8**:433, 1930.

The distribution of dyestuff varies according to the length of time after its injection. In the first period it is distributed to the blood and lymph and to the tissue, and is being excreted by the liver and kidney. In the second period the dye can no longer be seen in the blood stream. The isolated dye is excreted through the liver, concentrated to a visible degree. The amount of the injection, the interval of time after the injection and the functional state of the storing cells constitute the factors for the granular storage of congo red in the reticulo-endothelial cells. A close relationship exists between these factors.

EDNA DELVES.

Pathologic Chemistry and Physics

POSTOPERATIVE BLOOD CHEMISTRY. E. ANDREWS and K. REUTERSKIOLD, Ann. Surg. **92**:786, 1930.

Intensive postoperative chemical studies of the blood were made on patients from twenty-four to thirty-six hours after operation. There were no significant changes in the leukocytes, blood pressure, temperature, pulse rate, blood sugar,

water content, chlorides or carbon dioxide. Marked changes were found in the Aldrich-McClure test indicative of increased tissue thirst. Tests of permeability of the skin showed that this was much increased. Profound changes in the balance of mineral salt were noted. The potassium calcium ratio often fell below one. These changes per se may be considered adequate to account for the condition known as postanesthesia sickness.

AUTHORS' SUMMARY.

ACETONE BODIES IN NORMAL PREGNANCY AND IN THE TOXEMIAS OF PREGNANCY. H. J. STANDER and J. F. CADDEN, Bull. Johns Hopkins Hosp. **47**:382, 1930.

The total acetone bodies (free acetone, diacetic acid and beta-oxybutyric acid) in the blood in normal nonpregnant women vary between 11 and 18 mg. of acetone per liter of blood, after correction for lactic acid, the average being 15.8 mg. In normal pregnancy the total corrected acetone bodies vary between 11 and 24 mg. per liter of blood, with an average slightly higher than in the nonpregnant woman (16.6 mg.). The total corrected acetone bodies in the blood of pregnant women with nephritis lies between 8.6 and 48.8 mg. of acetone per liter of blood. Eclampsia is accompanied by a definite elevation in the quantity of acetone bodies in the blood, averaging 50.2 mg. of acetone per liter of blood. The tendency toward ketosis in pregnant women may in part explain the lowered total base observed in their blood as term is approached. The increased acetone bodies in the blood of eclamptic patients may be a partial factor in producing the uncompensated deficit of alkali seen in that disease, although the accumulation of lactic acid is perhaps the major factor in the causation of the acidosis. A diet low in fats and high in carbohydrates seems indicated in normal pregnancy, and must certainly be of value in cases of toxemias showing evidence of ketosis.

AUTHORS' SUMMARY.

THE ELIMINATION CURVE OF IODINE FROM THE BLOOD. H. EITEL and A. LOESER, Klin. Wchnschr. **10**:109, 1931.

The elimination curve of iodine from the circulating blood following the intravenous administration of sodium tetraiodophenolphthalein during ten hours is a regular decline. After ligation of the ductus choledochus, there is an initial decline and then a marked delay in the elimination of iodine. After ligation of the cystic duct, there is an irregular elimination of iodine, so that a steplike curve is formed.

AUTHORS' SUMMARY.

TRACES OF MERCURY IN THE URINE AND FECES. PAUL BORINSKI, Klin. Wchnschr. **10**:149, 1931.

The excrements of 51 per cent of seventy-five persons having no contact with mercury contained this metal. The daily excretion was from 5 to 10 γ (γ = 0.001 mg.). The same daily excretion of mercury was observed in persons with old amalgam fillings. Those with recent fillings, as well as those otherwise coming in contact with mercury, eliminated appreciably more. Practically all foods contain small traces of mercury; the amount ingested daily in food is estimated at 5 γ, an amount equal to that eliminated by persons having no contact with mercury or carrying old amalgam fillings. The average daily excretion of from 5 to 10 γ is considered normal and does not indicate poisoning with mercury.

AUTHOR'S SUMMARY.

THE SPECIFIC GRAVITY OF THE BLOOD AND ITS CONSTITUENTS. C. OESTREICH, Klin. Wchnschr. **10**:160, 1931.

The specific gravity of the whole blood varies from 1.050 to 1.060, and that of the plasma, from 1.025 to 1.026. In anemia, the specific gravity of the whole blood diminishes; it was observed as low as 1.030. A high specific gravity (from

1.095 to 1.100) of the red cells was observed in pernicious anemia. A specific gravity of the erythrocytes of over 1.095 indicates pernicious anemia; the normal is from 1.085 to 1.094.

AUTHOR'S SUMMARY (IN PART).

THE CHOLESTEROL OF THE BLOOD IN HYPERTENSION. C. ALVAREZ and S. M. NEUSCHLOSZ, Klin. Wchnschr. **10**:244, 1931.

The serum of normal persons is unsaturated (from 50 to 90 per cent) with reference to cholesterol. In hypertension it is supersaturated (from 106 to 132 per cent). Among twenty-five patients with hypertension, only four were without this change.

AUTHORS' SUMMARY.

Microbiology and Parasitology

THE ETIOLOGY OF RHEUMATOID ARTHRITIS. RUSSELL L. CECIL, EDITH E. NICHOLLS and WENDELL J. STAINSBY, Am. J. M. Sc. **181**:12, 1931.

The evidence for the streptococcal origin of rheumatoid arthritis may be summarized as follows: Almost constant presence of streptococci in foci of infection. Streptococci recoverable from blood in 62.3 per cent of rheumatoid patients; 3.9 per cent in pathologic controls; none in healthy controls. Streptococci recoverable from affected joints in 67.3 per cent of rheumatoid patients; from blood or joint in 77 per cent; none from nonrheumatoid joints. High agglutination of "typical strains" of streptococci with serums of 94 per cent of patients with rheumatoid arthritis. Disappearance of agglutinins with recovery from systems of arthritis. Biologic identity of streptococci recovered from blood, joint and focus of infection in the same patient, though there have been a number of exceptions to this rule. Reproduction of rheumatoid arthritis in rabbits with "typical strains" of streptococci. Recovery of same streptococcic from blood and joints of arthritic rabbits. Striking similarity of histologic changes in rabbits' joints to those in human rheumatoid joints.

AUTHORS' SUMMARY.

BRUCELLA INFECTION WITH RECOVERY OF BRUCELLA FROM THE BILE. HUGH R. LEAVELL and HAROLD L. AMOSS, Am. J. M. Sc. **181**:96, 1931.

A case is described in which *Brucella* was recovered from the bile removed by duodenal drainage, and from the contents of the gallbladder at operation. In a patient whose extirpated gallbladder contained *Brucella*, the stools, from which *Brucella* was isolated prior to operation, no longer showed these organisms following cholecystectomy.

AUTHORS' SUMMARY.

STUDIES ON THE VIRUS OF FOWL-POX. E. W. GOODPASTURE, A. M. WOODRUFF and C. E. WOODRUFF, Am. J. Path. **6**:699 and 713, 1930.

Fowlpox virus in suspensions of finely divided material is rendered inactive after a period of from four to twenty-four hours in 1 per cent potassium hydroxide. In the form of inclusion bodies, however, the virus is found to be infectious, in diminishing strength, after treatment with potassium hydroxide for as long as five days. No evidence has been found for the existence of a nucleoproteid toxin, such as that described by Sanfelice, either in scabs of the fowlpox lesion or in digested inclusion bodies. The destructive action of 1 per cent potassium hydroxide on normal epithelial cells of the chick is shown. The presence of Borrel bodies in inclusion which have been proved infectious after remaining twenty-four hours in 1 per cent potassium hydroxide has been demonstrated.

Inclusion bodies of fowlpox may be broken up by using the surface tension of a drying film of water. The stained smear of an inclusion body thus disrupted has been shown to contain as many as 20,000 Borrel bodies—minute coccoid structures uniform in size and shape. Multiple inoculations have been made from

the smears of isolated and ruptured inclusion bodies with as many as six inoculations from a single inclusion resulting successfully. Control inoculations were all negative. The lipoid component of the inclusion bodies is noninfectious. Aside from this lipoid, the Borrel bodies form the major constituent of the inclusions and are judged to represent the actual virus of fowlpox.

AUTHORS' SUMMARIES.

THE INCLUSION BODIES OF FOWL-POX AND MOLLUSCUM CONTAGIOSUM. E. W. GOODPASTURE and C. E. WOODRUFF, Am. J. Path. **7**:1, 1931.

The inclusion bodies of molluscum contagiosum may be freed from surrounding cellular material by tryptic digestion. Unlike fowlpox inclusions, the molluscum bodies are found to be sticky and gelatinous after they have been digested. Because of this characteristic they cannot be manipulated readily with the Chambers microdissection apparatus. The gelatinous matrix of the molluscum bodies has a markedly granular appearance owing to the presence within it of myriads of Lipschütz granules—minute coccoid structures 0.25 micron in diameter. These granules are identical in size, shape and staining reactions with the Borrel bodies of fowlpox. They are resistant to the action of trypsin. On being placed in distilled water, the inclusion bodies of molluscum show little or no swelling. Under similar conditions the fowlpox inclusions swell markedly, owing, probably, to their lipoid material acting as a semipermeable membrane. Trituration of the molluscum inclusions readily breaks them up into the component Lipschütz granules. Fowlpox inclusions, similarly treated, fail to break up so readily into Borrel bodies. This difference in the reaction of molluscum and fowlpox to trituration may afford an explanation for the relatively greater filtrability of the former. Fowlpox and molluscum contagiosum are apparently specific for fowls and man, respectively, cross-inoculation experiments having proved unsuccessful. Attempts to transfer molluscum to monkeys and other laboratory animals were also unsuccessful.

AUTHORS' SUMMARY.

EXPERIMENTAL EFFORTS TO TRANSFER MONKEY MALARIA TO MAN. HERBERT C. CLARK and LAWRENCE H. DUNN, Am. J. Trop. Med. **11**:1, 1931.

We conclude that red spider monkey malaria and the human benign species of malaria that it so closely resembles are not identical, and that the monkey is not, therefore, a reservoir for human malaria, in view of the fact that in two control monkeys of different species from the red spider monkey acute attacks of malaria developed on schedule time (eleven days) and that no symptoms and no satisfactory laboratory observations developed in eight men representing the best type of nonimmune subjects. It remains to be seen, however, what may happen when an infant monkey (born free from opportunities to acquire monkey malaria) is inoculated with human malaria of the benign species. We await this opportunity, but circumstances indicate that it will not acquire the disease. The knowledge gained by our local field and laboratory work on monkeys offers one practical feature. The infant and juvenile monkeys of certain species (*Ateles* and *Cebus*) offer a better animal for sesearch in malaria than the bird, which is customarily used. It is interesting to note that two specimens of *A. tarsimaculatus* and one specimen of *A. albimanus* fed on the monkeys showed positive glands on dissection. Further work is indicated in feeding mosquitoes on monkey malaria since it may at least assist in providing teaching material.

AUTHORS' SUMMARY.

STUDIES ON YELLOW FEVER IN SOUTH AMERICA. NELSON C. DAVIS and RAYMOND C. SHANNON, Am. J. Trop. Med. **11**:21, 1931.

Aedes fluviatilis has been found to transmit yellow fever virus under laboratory condition. As few as three insects have produced a fatal infection by feeding on a rhesus monkey. *Aedes taeniorhynchus* has proved to be a less efficient

host than *Aedes fluviatilis*. However, in one instance a fatal infection of yellow fever resulted from the bites of this species. No transmission of yellow fever has been secured by the bites or by the injection of *Sabethine* mosquitoes. It is thought that in one instance yellow fever virus remained alive in the bodies of *Triatoma megista* for one week. However, the experiments with *Triatoma* have been rather inconclusive.

AUTHORS' SUMMARY.

THE TRANSMISSION OF YELLOW FEVER. NELSON C. DAVIS, Am. J. Trop. Med. **11**:31, 1931.

Stegomyia mosquitoes captured in houses in Sao Salvador, Bahia and Brazil did not produce yellow fever when injected into *Macacus rhesus*. Mosquitoes that had already digested a meal of immune blood gave rise to no immunity when injected into or fed on rhesus monkeys. Mosquitoes that had already digested one or more meals of immune blood became infective after feeding on an animal with yellow fever. In mosquitoes that had already digested a meal of infectious blood, the ingestion of immune blood had no influence on the subsequent development of infectivity. Two batches of mosquitoes that fed on a mixture of infectious blood and immune serum did not become infective. The mixture itself produced yellow fever when injected directly into a monkey. A similar blood mixture with saline solution substituted for the immune serum proved infectious on direct inoculation and gave rise to infectivity on ingestion by two batches of mosquitoes. Mosquitoes that took an interrupted meal, first on an immune monkey and immediately afterward on an infected monkey, developed infectivity. A similar lot, which fed first on the infected and secondly on the immune animal, produced no disease when injected into a rhesus monkey. However, the monkey was subsequently immune to a test dose of virus.

AUTHOR'S SUMMARY.

OCULAR LESIONS OF RAT-BITE FEVER IN GUINEA-PIGS. S. BAYNE-JONES and M. L. LERNER, Arch. Ophth. **4**:858, 1930.

Lesions of the eyes and contiguous structures occurred in about 60 per cent of guinea-pigs infected with *Spirochaeta morsus-muris*. The infection is reproducible with regularity in these animals and provides a convenient method for the investigation of ocular lesions occurring in the course of a systemic infection. The lesions vary in intensity during the course of the disease, but are generally severe at the time when the animals are moribund. The infection produces blepharitis, conjunctivitis, interstitial keratitis with corneal ulceration and moderate iritis and cyclitis. Characteristic cellular infiltratons occur also in the lacrimal glands, chiefly around the ducts, and in the perivascular regions in the external ocular muscles. Spirochetes were found in the conjunctival exudate, but could not be demonstrated with certainty in the cornea.

AUTHORS' SUMMARY.

THE ACTION OF LOW-VELOCITY ELECTRONS ON MICROÖRGANISMS. D. A. WELLS, Bull. Basic Sc. Research **3**:5, 1931.

Staphylococcus albus is killed when exposed to a beam of low velocity electrons. When the total energy is maintained at a constant value, there is a rapid rise in the percentage of killing within the range of from 25 to 30 volts. The results indicate that the lethal action is a function of the energy of the individual electrons.

C. E. CLIFTON.

THE INCREASED BACTERICIDAL EFFECT OF INORGANIC COMPOUNDS IN THE PRESENCE OF X-RAYS. R. F. NORRIS, Bull. Basic Sc. Research **3**:19, 1931.

When bacteria are irradiated with x-rays in solution containing various inorganic salts, the resulting lethal action is much greater than that obtained by

exposing the bacteria successively to x-rays and to the salts previously irradiated. Evidence is given to indicate that this is a true synergistic action and not primarily due to ultraviolet fluorescence, or to emission of photo-electrons.

C. E. CLIFTON.

THE CELLS FOUND IN TUBERCULOUS TISSUES ON VITAL AND SUPRAVITAL STAINING. E. H. TOMPKINS and R. S. CUNNINGHAM, Bull. Johns Hopkins Hosp. **48**:8, 1931.

Tissues from tuberculous guinea-pigs were stained vitally with trypan blue. The tissues were examined both by sections of fixed material and by scrapings stained supravitally. The large mononuclear cells found in the tuberculous areas consisted of monocytes, clasmatocytes and epithelioid cells, together with transitional and degenerate forms of the same cells. Only a few of the monocytes contained trypan blue, although they stained vigorously with neutral red. The clasmatocytes always contained trypan blue in great amounts. The number of epithelioid cells that contained the vital dye and the amount of dye within them varied considerably. By means of the superimposition of the supravital on the vital dye, transitions could be followed from clasmatocytes to epithelioid cells, as well as from monocytes to epithelioid cells. The types of staining observed in the giant cells were analogous to those observed in the mononuclear cells. The concept has been developed that, in tuberculosis, some toxic factor, acting either from within or from without the cells, affects the functions of both the monocytes and the clasmatocytes, so that these cells become modified both in morphology and in activity, and develop into characteristic epithelioid cells or into giant cells, or die and degenerate at any stage in the course of these changes.

AUTHORS' SUMMARY.

CONTROL OF INTESTINAL PUTREFACTION IN MAN BY DI-HYDRANOL. V. LEONARD and W. A. FEIRER, Bull. Johns Hopkins Hosp. **48**:25, 1931.

Intestinal putrefaction is usually a mild and irregular phenomenon, although instances in which it may be a constant and fairly active process are by no means uncommon. Since the organisms of true putrefaction are spore-bearers, the putrefactive properties of the stools may be taken as a measure of intestinal putrefaction. The presence or absence of intestinal putrefaction in a given case as well as its intensity may therefore be proved by simple, direct, bacteriologic methods. The administration of di-hydranol (2-4-dihydroxyphenyl n-heptane) in doses of from 0.3 to 0.45 Gm., three times daily, destroys the true putrefactive flora of the intestinal tract with great certainty and regularity.

AUTHORS' SUMMARY.

EXPERIMENTAL SYPHILIS. A. M. CHESNEY and T. B. TURNER, Bull. Johns Hopkins Hosp. **48**:90, 1931.

When rabbits are inoculated with syphilitic virus in such a manner as to produce a lesion involving the skin, whether the original inoculation is made subcutaneously, intracutaneously or by depositing the virus on the surface of a granulating wound, subsequent inoculation with homologous virus after a period of four months or more is not followed by the development of lesions, no matter whether the second inoculation is made intratesticularly, subcutaneously, intracutaneously or intravenously. Under these conditions, intravenous reinoculation may be followed by reinfection without lesions. When syphilis develops in rabbits after intratesticular inoculation, a second inoculation with homologous virus by the intracutaneous route after a period of four months or more is not followed by the development of any lesions at the site of inoculation. When syphilitic virus is injected intravenously into rabbits, marked and widespread lesions of the skin and bones develop. When these animals are reinoculated with homologous virus

after a period of several months, whether by subcutaneous or by intracutaneous injection, no lesions develop. However, intravenous injection under these circumstances may be followed by reinfection, but without lesions. The bearing of these facts on the distribution of acquired resistance in syphilis is discussed.

AUTHORS' SUMMARY.

THE GERMICIDAL ACTION OF α-MERCAPTO AND α-DISULFO SOAPS. A. H. EGGERTH, J. Exper. Med. **53**:27, 1931.

Certain of the α-mercapto soaps and α-disulfo soaps are powerful germicides. In the α-mercapto series, the soaps with 12 and 14 carbon atoms are most germicidal. In the disulfo series, the dicaprate, dilaurate and dimyristate are most germicidal. The optimum number of carbon atoms varies with the test organism used. These soaps, like others previously studied, show a markedly selective germicidal action.

AUTHOR'S SUMMARY.

THE ACTION OF TESTICLE, KIDNEY, AND SPLEEN EXTRACTS ON THE INFECTIVE POWER OF BACTERIA. M. PIJOAN, J. Exper. Med. **53**:37, 1931.

The addition of testicle extract to cultures of twenty different bacteria just prior to inoculation enhances their infectious activity to a high degree. Kidney extracts enhance the infections of staphylococci to a less degree than testicle extracts, while spleen extracts never give rise to enhancement and often cause the lesion to be less severe than would ordinarily be the case.

AUTHOR'S SUMMARY.

THE EFFECT OF TESTICULAR EXTRACT ON FILTRABLE VIRUSES. D. C. HOFFMAN, J. Exper. Med. **53**:43, 1931.

The Reynals factor promotes the pathogenic action of the viruses of herpes, vesicular stomatitis of horses, Borna's disease and vaccinia. The heightening of virulence is revealed in various ways. The effects of the viruses may be accentuated, a weak strain may be converted into a strong one, as in the case of the F strain of herpes virus, or power may be acquired to infect resistant species or tissues, such as rabbits and the abdominal skin of guinea-pigs, with acute vesicular stomatitis. The Reynals factor should serve as an important agent in the study of filtrable viruses.

AUTHOR'S SUMMARY.

THE TOXIC PROPERTIES OF TUBERCULO-PROTEINS AND POLYSACCHARIDES. F. R. SABIN, F. R. MILLER, C. A. DOAN and B. K. WISEMAN, J. Exper. Med. **53**:51, 1931.

The temperature reaction in tuberculous and normal guinea-pigs and rabbits is elicited by the tuberculoprotein and probably not at all by the polysaccharides The polysaccharides may have some killing power under certain conditions, but this is not as consistently related to dosage as in the case of the proteins. Both proteins and polysaccharides cause a change in the white blood cells when introduced by any route.

AUTHORS' SUMMARY.

AN ACCELERATED FEBRILE REACTION IN MONKEYS UPON REINOCULATION WITH POLIOMYELITIS VIRUS. C. W. JUNGEBLUT, J. Exper. Med. **53**:159, 1931.

As a rule, primary poliomyelitic infection in the monkey, is not characterized by a significant increase in the temperature of the body during the incubation period until forty-eight or twenty-four hours before the onset of clinical symptoms, when a critical rise of the temperature occurs. On intracerebral reinoculation, the temperature curve of recovered monkeys shows an almost immediate and

marked febrile reaction during the first twenty-four or forty-eight hours after inoculation. A similar accelerated febrile reaction may be obtained in recovered animals after subcutaneous injection of killed virus. In case the previous infection is of recent date, reinoculation may not lead to demonstrable reaction. Monkeys that have received a number of parenteral injections of live virus respond to intracerebral infection with a precocious and prolonged febrile reaction on the third or fourth day after infection, which may last until the onset of symptoms. The altered response to reinoculation of monkeys that have previously been in contact with the virus suggests a close analogy with the accelerated reactions observed in allergic phenomena.

AUTHOR'S SUMMARY.

LESIONS IN THE CENTRAL NERVOUS SYSTEM IN HOG CHOLERA. O. SEIFRIED, J. Exper. Med. **53**:277, 1931.

A more or less marked encephalomyelitis and meningitis was found in thirty-three of thirty-nine cases of virus hog cholera in which the animals had been infected either intramuscularly or by contact and killed between six and forty-nine days after infection. This hog cholera encephalitis is characterized by a varying amount of vascular and perivascular infileration with small lymphocytes, mononuclear elements, a few plasma cells and occasionally a few eosinophilic leukocytes. The glia shows a proliferation surrounding infiltrated vessels or forming small nodules or more diffuse foci. Satellitosis and, in a few instances, true neuronophagia have been observed. Both microglia and macroglia participate in this process. There is no essential increase of glia fibers. In nearly all parts of the central nervous system degenerating lesions of the nerve cells, such as tigrolysis and degeneration of the nucleus, including a slight atrophy of endocellular neurofibers, are encountered. No demyelinization has been observed. Specific inclusion bodies in the nerve cells are absent. In addition, in a certain number of cases microscopic and macroscopic hemorrhages are present in the brain, spinal cord and meninges. These lesions, in varying degrees, have been found in swine infected with four different strains of hog cholera virus. Two were laboratory strains and two were obtained from fresh field outbreaks. Histologic changes in the central nervous system were found as early as six days after infection before the animal showed symptoms in the central nervous system. In two cases in which the animals were paralyzed, no lesions could be demonstrated in the central nervous system. The lesions in the central nervous system are considered to be the anatomic substratum for the various nervous symptoms commonly found in hog cholera.

AUTHOR'S SUMMARY.

THE VIABILITY OF BOVINE TUBERCLE BACILLUS ON PASTURE LAND, IN STORED FAECES AND IN LIQUID MANURE. R. STENHOUSE WILLIAMS and W. A. HOY, J. Hyg. **30**:413, 1930.

Under ordinary conditions in the south of England, *B. tuberculosis* may remain alive and virulent in cow feces exposed on pasture land for at least five months during winter, for two months during spring and for four months during autumn. In summer no living organisms were demonstrated after two months. Under special conditions, e. g., protection from direct sunlight, the survival period may be four months during the summer. In the autumn, feces protected from earthworms, etc., yielded bacilli after six months. Living and virulent tubercle bacilli were found after twelve months' storage in the naturally infected feces, and for a period of at least two years in the artificially infected feces. Living and virulent tubercle bacilli were found in stored liquid manure at least four months after infection. During this time a gradual diminution of the virulence of the material was observed.

AUTHORS' SUMMARY.

THE PATHOLOGY OF GENERALIZED VACCINIA IN RABBITS. RALPH D. LILLIE and CHARLES ARMSTRONG, Nat. Inst. Health Bull., 1930, no. 156.

An account of the pathologic histology of local and focal lesions of the skin, mucosæ and viscera of rabbits produced by Armstrong's heat-selected vaccine virus is detailed. The literature of the histology of variola and vaccinia is reviewed. The visceral lesions are essentially coagulation necroses; those of the skin and mucosae also show coagulation necrosis in addition to various other proliferative, degenerative, hemorrhagic and inflammatory changes. The distribution of such focal lesions is summarized in tabular form according to organs and by routes of inoculation and lapse of time after inoculation.

AUTHORS' SUMMARY.

BACILLUS PSITTACOSIS NOCARD, 1893: FAILURE TO FIND IT IN THE 1929-30 EPIDEMIC IN THE UNITED STATES. SARA E. BRANHAM, GEORGE W. MCCOY and CHARLES ARMSTRONG, Pub. Health Rep. **45**:2153, 1930.

During the recent outbreak of psittacosis in the United States, an intensive search for the *"Bacillus psittacosis"* of Nocard was made in the carcasses and droppings of parrots that were shipped to the National Institute of Health, in experimentally infected and in normal parrots and parrakeets, and in material obtained from human cases. No strain of *"B. psittacosis"* or of any other member of the *Salmonella* group of bacteria was found. In fifty-seven convalescent serums studied, agglutinins for *"B. psittacosis"* and other *Salmonella* bacteria were not demonstrable in dilutions that could be considered significant. We have found no evidence of the association of any member of the *Salmonella* group of microorganisms with psittacosis either in birds or in man.

AUTHORS' SUMMARY.

THE TRANSMISSIBILITY OF TICK-BITE FEVER VIRUS TO GUINEA PIGS. ADRIANUS PIJPER and HELEN DAU, Brit. J. Exper. Path. **11**:287, 1930.

We believe we have shown that it is possible to transmit the virus of South African tick-bite fever to guinea-pigs. The animals react with a rise of temperature. In one instance, we have reached the fifth animal passage. Passages seem to increase the virulence. At postmortem examinations of our animals we have looked for, but have not found, evidence that perhaps some other, accidental, infection had been transmitted by us. Our temperature curves resemble those usually recorded, and regarded as typical, for guinea-pigs infected with *Rickettsia* virus (typhus and spotted fever of the Rocky Mountains). On these, and other grounds, also given in this paper, we conclude that South African tick-bite fever is caused by a living virus of the *Rickettsia* class.

AUTHORS' SUMMARY.

CHANGES IN THE CENTRAL NERVOUS SYSTEM OF MONKEYS DUE TO VACCINE LYMPH. P. A. CLEARKIN, Brit. J. Exper. Path. **11**:329, 1930.

Perivascular lesions have been found in the central nervous system of a large number of wild African monkeys after intradermic inoculation with vaccine lymph. The severity of the lesion depends to some extent on the dosage. The histology of the severe lesions is similar to that of postvaccinal encephalitis in man. This supports the view that vaccinia is the cause of postvaccinal encephalitis.

AUTHOR'S SUMMARY.

A SALMONELLA CAUSING ABORTION IN SHEEP. R. LOVELL, J. Path. & Bact. **34**:13, 1931.

Several strains of *Bacterium abortus-ovis*, a *Salmonella* organism causing epidemic abortion in sheep, have been studied in regard to their morphology, cultural and fermentation reactions and antigenic structure. The British strains

and the one of German origin ferment dextrose, maltose, mannite, xylose and dulcite, with the production of gas. All of the strains studied failed to attack lactose, sucrose, salicin, inosite, rhamnose and, with rare exceptions, arabinose. All of the strains produced hydrogen sulphide slowly. The antigenic structure of the five British strains and the one German strain appears to be identical. As regards the "H" (flagellar) agglutinogens, *Bact. abortus-ovis* is diphasic. The main component of the type phase is shared with *Bact. paratyphosum C*. With regard to the group phase, an important factor is shared with *Bact. paratyphosum C* and the related varieties, but there is also an additional component that appears to be peculiar to *Bact. abortus-ovis*. The "O" (somatic) antigens are shared with *Bact. abortus-equi* and the Reading and Derby types. One of the minor factors is shared with *Bact. enteritidis*.

AUTHOR'S SUMMARY.

OBSERVATIONS ON TROPICAL TYPHUS IN THE FEDERATED MALAY STATES. R. LEWTHWAITE, Bull. Inst. M. Research, Federated Malay States, 1930, no. 1.

Tropical typhus differs from the typhus of the western world in two ways. It is not louse-borne and it does not flare up in devastating epidemics. Two types are described, the "K" or "rural" and the "W" or "urban." These types are distinguishable only by epidemiologic and serologic methods. Tropical typhus is an acute infectious disease characterized by an abrupt fever and severe headache. A rash, macular and papular, appears after about five days, and the crisis appears at the end of the second week. Clinically, it resembles typhus exanthematicus, but epidemiologically it resembles other typhus-like fevers of the tropical region. It is a disease of inland towns and the countryside, the greatest percentage being of the "rural" type. Occupation greatly influences the incidence, and very few children are infected. The incidence is higher in males than in females. All cases, but one, gave positive Weil-Felix reactions. An excellent discussion of signs and symptoms, morbid anatomy and histopathology is included. In the study of the epidemiology of tropical typhus, little seasonal variation was found. Also, it was found that the "urban" type was largely a disease of indoor workers, while the "rural" type attacks those whose occupation involves contact with the countryside, especially the waste land overgrown with underbrush.

EDNA DELVES.

EXPERIMENTAL TROPICAL TYPHUS IN LABORATORY ANIMALS. R. LEWTHWAITE, Bull. Inst. M. Research, Federated Malay States, 1930, no. 3.

In only a small number of cases does the inoculation of the tropical typhus virus cause a febrile reaction in guinea-pigs. Rats were found more susceptible. The intraperitoneal inoculation of infected human blood into rats produced a febrile reaction, but the results were not constant. A fever did not develop in all of the rats thus treated. However, in those in which a fever did develop, the postmortem changes were fairly constant. Enlargement of the spleen was found in most of the rats in which a fever developed. In one of the five rats examined histologically, perivascular infiltration and typhus "nodules" were found in the brain. In another of the five cases, clumps of short diplobacilli with tapering ends were found in the brain. They seem to resemble the "diphtheroid" in morphologic appearance. Three of the eleven rabbits tested gave positive Weil-Felix reactions after being inoculated with infected human blood.

EDNA DELVES.

SEPTINEURITIS IN NEUROTROPIC VIRUSES. S. NICOLAU, O. DIMANCESCO NICOLAU and I. A. GALLOWAY, Ann. de l'Inst. Pasteur **43**:1, 1929.

Septineuritis refers to the general spread of neurotropic viruses by way of the central, visceral or peripheral nervous system, with lesions in the trunks and finer nerve endings. Experimentally, it may be reproduced in animals with the

virus of encephalomyelitis or Borna's disease, smallpox, herpes, poliomyelitis and fixed or street rabies virus. The histologic picture (two color plates and twelve figures) is stated to show definite dissemination with accompanying lesions by way of the nervous system. The report is eighty-eight pages in length.

M. S. MARSHALL.

POLIOMYELITIS IN ROUMANIA IN 1927. G. MARINESCO, M. MANICATIDE and S. DRAGANESCO, Ann. de l'Inst. Pasteur **43**:223, 1929.

More than 1,500 cases are reported; they were studied clinically, therapeutically and from the standpoint of gross and cellular pathologic changes. The morbidity showed a peak in incidence between the ages of 1 and 3 years (61.9 per cent), and a ratio of 3:2 in males over females; the mortality was around 9.5 per cent. The report covers fifty-five pages and is quite complete.

M. S. MARSHALL.

VARIABILITY IN SKIN FUNGI. R. BILTRIS, Ann. de l'Inst. Pasteur **43**:281, 1929.

In an article of 61 pages a mycologic study, accompanied by seventy-nine photographs, is presented on the characteristics of the dermatophytes. The question of morphologic and cultural variation is emphasized, particularly in the *Trichophyton* genus.

ENCEPHALOMYELITIS PROVOKED BY TOXOPLASMA CUNICULI. C. LEVADITI, V. SANCHIS-BAYARRI, P. LÉPINE and R. SCHOEN, Ann. de l'Inst. Pasteur **43**:673, 1929.

Toxoplasmic encephalomyelitis in rabbits may run a chronic course in which the neuraxon continues to be contaminated by encysted *Toxoplasma* (schizonts), resembling the parasitic cysts described in human hydrocephalus (Jankû); toxoplasmic encephalomyelitis in mice may also evolve chronically. Certain animals live for 165 days and appear normal in spite of intense alterations of which the neuraxon is the seat, and although they are carriers of organisms virulent for the rabbit. (Sixty-two pages, with seven figures in color.)

AUTHORS' CONCLUSIONS.

ENCEPHALOMYELITIS PROVOKED BY TOXOPLASMA CUNICULI. C. LEVADITI, V. SANCHIS-BAYARRI, P. LÉPINE and R. SCHOEN, Ann. de l'Inst. Pasteur **43**:1063, 1929.

The study of encephalomyelitis induced in the rabbit, guinea-pig, pigeon, mouse and rat by *Toxoplasma cuniculi* furnishes particularly interesting results with reference to human pathology. It is correlated with certain etiologic problems in the domain of neuropathology, particularly those related to hydrocephalus and to certain hereditary congenital encephalites. The certainty of penetration of some of these protozoa in the cytoplasm of the neurons (neuroprotozooses) is furnished by the statements summarized in our articles. It renders more and more reasonable the microsporidian nature of the rabies virus, the Negri bodies of which represent, according to us, evolutionary phases (pansporoblastic phase) of *Gluglea lyssae* (Levaditi, Nicolau and Schoen). Finally, our investigations permit an explanation of the mechanism of immunity acquired from the neuraxon as exclusively a tissue immunity, eminently vital and independent of the parasiticidal properties of humoral substances.

AUTHORS' CONCLUSIONS.

VACCINE VIRUS IN THE MONKEY. H. ALDERSHOFF, A. B. F. A. PONDMAN and A. W. POT, Ann. de l'Inst. Pasteur **43**:1268, 1929.

The brain of the *Cynomolgus* monkey responds to different vaccine viruses. Neurovaccine has no particular affinity for the neural axis of this animal. The virus may be cultivated in the brain without loss of virulence. Monkeys may be

vaccinated so effectively that intracerebral inoculation causes no trouble. Animals refractory to an intracerebral injection of neurotropic rabbit virus (from an infant dying of postvaccinal encephalitis) succumb, after an intracerebral reinjection with a fixed virus, to a paralysis caused by the latter. The hemorrhagic reaction, produced following cutaneous vaccination with neurotropic rabbit virus, is not a typical characteristic of this virus, but is observed also after cutaneous vaccination with the vaccine virus cultivated in the testicles of rabbits or in the brain of the monkey. We presume that this hemorrhagic reaction is a specific property of all vaccine viruses cultivated in tissues other than the skin. This factor will be investigated further. (Comment is made on this paper by C. Levaditi, ibid., p. 1512.)

AUTHORS' CONCLUSIONS.

THE LYMPHOCYTE-MONOCYTE RATIO IN TUBERCULOUS INFECTION. T. DE SANCTIS MONALDI, Ann. de l'Inst. Pasteur **44**:70, 1930.

The injection of filtrates ("ultravirus") of tuberculous material, active bacilli, heated ultravirus (80 C.), tuberculin and B C G into guinea-pigs was followed by hematologic studies. The author concludes: The blood picture in animals inoculated with ultravirus should be divided into two types, one in which the lymphocyte-monocyte ratio remains high in animals overcoming infection, and the other with a descending ratio in dying cachectic animals, with enlarged lymph nodes in which acid-fast organisms are shown by repeated passage. The white cell count and the lymphocyte-monocyte ratio of the latter group are similar to those of guinea-pigs given injections of virulent organisms. With B C G, the picture simulates conditions obtaining in animals recovering from infection with ultravirus. The lymphocyte-monocyte ratio may double within two or three months, indicating a good prognosis. A large number of nonmotile cells are produced during the marked leukocytosis and cachexia in animals succumbing to virulent organisms or to ultravirus. Some days before death, in these animals (only), monocytes appear, with a small central roset and vacuoles dispersed through the protoplasm. The great number of nonmotile cells and these distinctive monocytes do not appear in animals inoculated with tuberculin or with B C G. The leukocyte reactions in animals inoculated with tuberculin or with heated ultravirus present quite a different picture from that described.

M. S. MARSHALL.

Tumors

BENIGN POLYMORPHOCELLULAR TUMORS OF THE KNEE REGION. W. C. HUNTER, Am. J. Path. **7**:13, 1931.

Two instances of benign polymorphocellular tumors occurring in the region of the knees of closely related persons are described. In the daughter, the new growth originated in the synovial membrane, a rare site of formation of a tumor, and was benign. In the father, the tumor was of exceptionally long duration, attained bulky dimensions and although exhibiting locally destructive properties also appeared to have been benign. Because of the large size and extensive ramifications of the mass, the point of origin could not be determined, but certain facts point to an extra-articular source. Most commonly new growths of the type herein reported arise from the sheaths of tendons and only rarely from the capsule or synovial membrane of the joints. In the latter event the knee is much more frequently involved than any other joint in the body. The rarity of such growths in the joint is evidenced by the fact that the author was able to collect from the literature, in addition to his own cases, only forty-four instances of closely similar or identical tumors.

AUTHOR'S SUMMARY.

HYPERNEPHROMA WITH TUMOR THROMBOSIS OF VENA CAVA AND HEART. S. H. POLAYES and H. TAFT, Am. J. Path. **7**:63, 1931.

This is the fifth case of hypernephroma with malignant thrombosis by invasion of the inferior vena cava and the heart. It is unique in its extent of involvement. The entire inferior vena cava and all its main tributaries (iliac, renal and hepatic veins) were occluded by a continuous malignant thrombus which extended into the right atrium, through the tricuspid valve into the right ventricle. The cardiac involvement here was even more extensive than in the case described by Weber, in which the thrombus did not extend beyond the right atrium. Another interesting feature was the fact that in spite of the massive involvement of the inferior vena cava and the right kidney, the right adrenal gland remained singularly free from metastasis.

AUTHORS' SUMMARY.

RESISTANCE AND SUSCEPTIBILITY TO CANCER. W. CRAMER, Ann. Surg. **93**:20, 1931.

At its inception cancer is beyond doubt a local disease that arises in a limited area of cells subjected to chronic irritation. However, the process of cancerization is one that does not arise merely as the result of a direct action of a carcinogenic agent on epithelial cells, but it is much more complex. In fact, the local development of a malignant condition is influenced by factors that do not reside in the epithelial cells, but in the organism, and exert their activity presumably through the system of the mesenchymal cells. The terms "susceptibility to cancer" and "resistance to cancer" are intended to embrace the activity of these factors. Furthermore, the study of these factors may enable one to modify their activity in such a way as to delay, or even to prevent, the inauguration of a cancer.

B. M. FRIED.

HEREDITY AND CANCER. H. T. DEELMAN, Ann. Surg. **93**:30, 1931.

According to Deelman, with Denmark and Switzerland, Holland, has the "doubtful privilege" of being at the head of a series of countries with the highest mortality rate from cancer. In his investigation on the heredity of cancer, the Dutch scientist asked the following question, In general, does cancer occur more frequently in the family of patients with cancer than in any other family in which there are at the moment no patients with cancer? The study is based on 250 gastric cancers collected over a period of three years.

Deelman's conclusions are as follows: 1. In a series of families of patients with cancer, cancer occurs more frequently than in any other series of families. 2. The surplus of cancer in the family of patients with cancer always accumulates in certain distinct families. 3. There is a large group of patients with cancer in whose family cancer is absolutely not more frequent than agrees with the "normal" chance of dying of cancer. 4. Hereditary influences are evident only in a small category of cases of cancer. 5. So far as can be judged from the material, there is no difference between the groups alluded to in 3 and 4 in regard to the localization of the primary tumor.

B. M. FRIED.

THE INTERRELATION BETWEEN HEREDITARY PREDISPOSITION AND EXTERNAL FACTORS IN THE CAUSATION OF CANCER. MAUD SLYE, Ann. Surg. **93**: 40, 1931.

During 14,000 necropsies, 1,301 neoplasms were found; of these 51 arose under observation at the sites of recorded gross trauma. In addition to these mice, in which there was involvement in external sites, there were 3 male mice in which tumor of the liver developed, each of which had been wounded and deeply bruised subcutaneously, immediately over the location of the tumor of the liver. It is interesting that within a stock of "noncancerous" strains identical gross traumas have occurred as frequently as in the cancerous strains without in any case leading to the formation of a neoplasm.

The article, which is the first of a series to be published, is illustrated with typical protocols. Slye concludes that in her material hereditary predispositions and external gross traumas were the interrelated causes of the occurrence of cancer.

B. M. FRIED.

EPITHELIAL METAPLASIA AND ITS RELATIONSHIP TO TUMORS. G. ROUSSY and C. OBERLING, Ann. Surg. **93**:90, 1931.

The opinion of the authors is that metaplasia should not be regarded as a precancerous lesion. It is common knowledge that metaplasia of the epithelium often occurs in organs following the development of a cancer. Thus in the gallbladder and in the uterus metaplasia of the epithelium is exceedingly rare in normal conditions, whereas metaplastic (heterotopic) tumors are not so uncommon. From the practical point of view, the interpretation of epithelial metaplasia should vary according to the organ involved. Whereas in the bronchus, the pancreas and the epididymis metaplasia does not signify imminent cancerization, in the uterus the finding of islands of heterotopic (malpighian) tissue is often a sign of a condition of cancerization.

B. M. FRIED.

EPIDERMOID CARCINOMA IN SEBACEOUS CYSTS. EVERETT L. BISHOP, Ann. Surg. **93**:109, 1931.

The development of carcinoma in the wall of a "wen" is probably less rare than is commonly believed. A good discussion of these cancers is given, with illustrative photomicrographs.

B. M. FRIED.

INTRACRANIAL CARCINOMATOUS METASTASES. R. MEAGHER and L. EISENHARDT, Ann. Surg. **93**:132, 1931.

Of 1,850 verified intracranial tumors, 57 (or 3 per cent) were metastatic, and of these 44 (2.3 per cent) were carcinomatous. The average age of the patients with intracranial metastases of the breast was 51 years, the oldest being 65, and the youngest 30. The onset of the intracranial signs after the primary focus in the breast averaged over three and one-half years, the interval ranging from three months to twelve years. The course from the appearance of intracranial symptoms was rapid, fatality ensuing on an average in six months, and operative intervention was survived on an average for six weeks, the longest period being five months.

B. M. FRIED.

THE GENETIC NEOPLASTIC RELATIONSHIPS OF HODGKIN'S DISEASE, ALEUKEMIC AND LEUKEMIC LYMPHOBLASTOMA, AND MYCOSIS FUNGOIDES. ALDRED SCOTT WARTHIN, Ann. Surg. **93**:153, 1931.

The presentation is based on 100,000 specimens examined between the years 1895 and 1927. Warthin is of the opinion that Hodgkin's disease is a neoplasm, being related genetically to the lymphoblastomas, of which both the aleukemic and the leukemic forms (mycosis fungoides) are identical pathologically. They all take their origin from perivascular reticulo-endothelium, or the maternal lymphoblasts of the lymphoid tissues of the body. They show true infiltrations and metastases. In their cell types and architecture they follow definite patterns which cannot be explained on the basis of an inflammatory reaction.

B. M. FRIED.

STUDIES IN HODGKIN'S DISEASE. ELSIE S. L'ESPERANCE, Ann. Surg. **93**:162, 1931.

The granulomatous character of the typical lesions speaks in favor of the conception that Hodgkin's disease is tuberculous. The author relates experiments to the effect that the avian tubercle bacillus is most likely the causative agent of

the disease. Experiments on the inoculation of chickens with an emulsion of lymph nodes from two patients with established Hodgkin's disease are described. The author is of the opinion that if animal inoculations were pursued consistently along the lines of recent investigations it would determine the tuberculous nature of at least one form of Hodgkin's disease.

B. M. FRIED.

SUSCEPTIBILITY AND RESISTANCE TO TAR CANCER. J. MAISIN, Ann. Surg. **93**: 180, 1931.

Maisin is of the opinion that cancer caused by tar results not only from local irritation, but from a general intoxication of the organism as well. Mineral salts, such as magnesium and copper, when given in convenient doses, are capable of delaying the appearance of cancer and of lowering the percentage of induced tumors. Salts of radioactive metals have an opposite effect. Diet can influence the appearance and evolution of cancer caused by tar. Thus a diet of liver accelerates the evolution of cancer caused by tar. Preceding closely the development of cancer caused by tar and during its evolution the metabolism of fats is deficient and the variations of the cholesteremia are marked. The same variations are to be noticed after repeated injections of ionium.

B. M. FRIED.

CARCINOMATOUS GASTRIC POLYP. T. GRIER MILLER, E. L. ELIASON and V. W. M. WRIGHT, Arch. Int. Med. **46**:841, 1930.

Carcinomatous polpy of the stomach is more frequent than has been generally believed, having been found in 35 per cent of all the cases of intragastric polyp that we have studied adequately (eight of twenty-three), and both the history and the pathologic data suggest that it usually originates in polyp of a benign nature. The benign intragastric polyps that show this tendency to malignant change are usually of an adenomatous construction. Most of the patients showing such malignant change are males (83 per cent), and the age incidence is the same as for mural gastric cancer. The symptoms are those of any malignant gastric lesion with, in addition, those of the two other common consequences of gastric polyp—intermittent pyloric obstruction and hemorrhage. The hemorrhage may be frank or occult; it not infrequently leads to an erroneous diagnosis of primary anemia (three of our eight personal cases). Consequently, gastric polyp should be considered in all cases of unexplained anemia. Roentgenologic study alone often makes the diagnosis of gastric polyp, and malignancy may be suspected on the basis of the clinical picture. Gastric polyp may be overlooked at operation, and special procedures, including gastrotomy and exploration of the interior of the stomach with a gastroscope, are indicated when any clinical suspicion of a polyp exists or when a suspected ulcer is not found. All gastric polyps, when demonstrated, deserve the radical surgical treatment commonly employed in cases of known or suspected gastric carcinoma.

AUTHORS' SUMMARY.

CARCINOMA OF THE STOMACH IN A SEVENTEEN YEAR OLD GIRL. A. MARBLE, Bull. Johns Hopkins Hosp. **48**:39, 1931.

An adenocarcinoma with metastases in the regional lymph nodes, removed at operation from a girl of 17 years, is described. The duration from the onset of symptoms was thirty-three months. Partial gastrectomy was made twenty-two months before death.

PRINCIPLES OF PROGNOSIS IN CANCER. WILLIAM C. MACCARTY, J. A. M. A. **96**:30, 1931.

I think it may be said scientifically that any system of microscopic grading of cancer should not alone be of accurate clinical value without taking many other factors into consideration. Furthermore, any system which merely states that

a certain percentage of patients with certain grades live a certain length of time does not necessarily furnish data for any specific case. In other words, there is no criterion by which one can state that a given case belongs in the favorable or unfavorable percentage. Moreover, the wise and successful practitioner of the art of medicine will certainly take all possible factors into consideration in making a clinical prognosis.

These practical clinical generalizations should not inhibit or prohibit pure scientific studies of possible factors which may or may not be indexes of behavior rather than prognosis in cancer. Perhaps these indexes might be of clinical value in the future, but at present all grading of cancers should be considered in the investigative or experimental stage.

AUTHOR'S SUMMARY.

THE DEVELOPMENT OF CANCER IN SCARS FROM BURNS. N. TREVES and G. T. PACK, Surg. Gynec. Obst. **51**:749, 1930.

Epidermoid carcinoma developed in 2 per cent of 2,465 patients with carcinoma of the skin, and in 0.3 per cent, in which, the tumors were of the basal cell type, the tumor originated on skin subjected to thermal injuries. This latter type occurred in instances wherein the burn was sufficiently superficial to spare the hair follicles and sweat glands. The age of the scar is more important than the age of the person, because this variety of cancer may occur in young people if the scar has existed for a long time, as from infancy or childhood. Scars accompanied by ulcers, fistulas, rhagades and adhesions establish an abnormal relation between epithelial and connective tissues and predispose to carcinomatous formation. Malignant changes in these scars are often multiple and may invade the surrounding scar, muscles, tendons and bones and extend by direct growth along the deep fascial planes. The lesion may be flat, indurated, infiltrative, ulcerative or evertent, assuming a papillary character. In the early stage, the carcinomatous process appears in the scar as an enlarging warty or scaling papule or in the form of a diffuse tumefaction, either of which may undergo ulceration in time.

RICHARD A. LIFVENDAHL.

MIXED TUMORS OF THE KIDNEY IN INFANCY AND CHILDHOOD. H. L. KRETSCHMER and W. G. HIBBS, Surg. Gynec. Obst. **52**:1, 1931.

Seventeen embryonal renal tumors are described. The tumor was bilateral in two cases. The kidney takes no part in the formation of the tumor. Glandular elements are always present; smooth and striated muscle, cartilage, fat and elastic, fibrous and myxomatous tissue are nearly always present. Embryonic tubules embedded in a heterogeneous matrix are the most conspicuous features. Metastases in the liver duplicate remarkably the typical new tubule formation, being arranged singly or in clumps.

RICHARD A. LIFVENDAHL.

CLASSIFICATION OF TUMORS. W. F. HARVEY and T. D. HAMILTON, Edinburgh M. J. **37**:609, 1930.

The classification advocated is of one into families, general, species and varieties, after the manner adopted in biology. Such a classification must conform to the ordinary rules of logical subdivision and naming. Especially is the error of a mixed basis for the formation of classes to be avoided and that of combining description with the genus, species or binomial terminology. The designations blastoma and cytoma may advantageously be substituted for malignant and non-malignant tumors and the time-honored names carcinoma and sarcoma may be abolished altogether. It is also recommended to do away with the designation papilloma in either a generic or a specific sense; papillary character is excluded from the name and relegated to the position of a descriptive character. Locality, tissue type and malignancy form the basis for the nomenclature recommended, and an attempt is made to put the principles advocated into practice by the presenta-

tion of a tentative classification of tumors. It is recognized that any such classification or a similar classification must first receive approval before it could ever be generally adopted.

AUTHORS' SUMMARY.

THE IMMUNOLOGICAL RELATIONSHIPS OF FOWL TUMOURS WITH DIFFERENT HISTOLOGICAL STRUCTURE. C. H. ANDREWES, J. Path. & Bact. **34**:91, 1931.

Six fowls bearing the slowly growing fibrosarcoma MH_1 have been found to have in their serum neutralizing properties active against filtrates of the Rous sarcoma no. 1. These serums would also neutralize filtrates of endothelioma MH_2 of the fowl. Similar neutralizing properties were found in the serum of only two of thirty-eight supposedly normal fowls. In birds bearing Rous sarcomas or MH_2 endothelioma, neutralizing antibodies may develop against the Rous virus in their serums, but the appearance of the neutralizing properties is far from constant.

AUTHOR'S SUMMARY.

HISTOLOGY AND HISTOGENESIS OF A FILTRABLE ENDOTHELIOMA OF THE FOWL. J. A. MURRAY and A. M. BEGG, Ninth Sc. Rep. Investigations of Imp. Cancer Research Fund, 1930, p. 1.

The tumor is transmitted by cell-free material. The cells of the new tumor are cells of the animal injected; the new tumor is a primary growth in the sense that cancer caused by tar is a new primary growth. The first indication of new growth is an accumulation of lymphocytes in the inoculated area which increase quickly in size and appear like macrophages. The macrophages proliferate by mitosis, become ameboid and throw off granular or vesicular portions of cytoplasm. Apparently in response to the setting free of a tumor agent, the susceptible cells of the area start to proliferate. It looks as if the tumor agent develops and increases in the macrophages. This conception is of interest in view of the mononuclear reaction in carcinoma.

CONGENITAL RHABDOMYOMA OF THE HEART. L. BERGER and A. VALLÉE, Ann. d'anat. path. **7**:797, 1930.

Multiple nodules of striated muscle, varying in size up to that of a small cherry, were found in the myocardium of a boy, aged 2 years. The tumors are regarded as congenital. The authors found forty-one cases of congenital rhabdomyoma recorded in the literature.

H. S. THATCHER.

ETIOLOGY OF TUMORS. M. MARULLAZ, Ann. de l'Inst. Pasteur **45**:443, 1930.

Analogies are drawn between the spontaneous malignant growth and those produced in the laboratory. A general discussion is presented, dividing tumors on the basis of cause as traumatic, spontaneous and functional (placental, etc.). The great importance of the nerve elements in the formation of neoplastic tissue is stressed. A note reports the death of the author some days after the receipt of this paper.

M. S. MARSHALL.

THE GRAFTING OF HUMAN CANCER ON THE CHIMPANZEE. J. TROISIER, Ann. de l'Inst. Pasteur **45**:660, 1930.

After numerous failures, I have once succeeded in transplanting a melanoma of the eye from a human being to a chimpanzee. Histologic examination has shown that the cellular elements of the transplanted melanoma were alive with their nuclei intact and their inclusions of melanin unmodified; the neoplastic tissue was compensated, and there was no adjacent lymphoconjunctival reaction. A certain local dissemination of the melanoma is clearly recognizable in the slides, but there were no metastases. If it is difficult to admit unreservedly that I have

inoculated a cancer disease of man to the anthropoid ape, it can nevertheless be said unequivocally that the heteroplastic graft of human neoplastic cells has been accomplished with the chimpanzee. In this sense it may be stated that the melanoma of man may be transferred to the chimpanzee.

AUTHOR'S CONCLUSIONS.

MIXED SQUAMOUS AND CYLINDRIC CELL CARCINOMA OF THE GALLBLADDER. W. ROESSIGER, Beitr. z. path. Anat. u. z. allg. Path. **85**:181, 1930.

According to the author, the literature contains records of only about thirty cases of pure squamous cell carcinoma of the gallbladder. To 1927, only eight cases of mixed carcinoma composed of both squamous and cylindric epithelial cells had been described. Roessiger reports three cases of such mixed carcinoma and one of squamous cell carcinoma. The fact that many carcinomas of the gallbladder are composed of cells that are indifferent in character and neither characteristically squamous nor columnar led him to postulate the presence of indifferent basal cells, in the mucosa of the gallbladder, in the sense of Krompecher. In surgically removed noncancerous gallbladders, he found cells that he holds to be basal cells. They occur singly or in small groups, not to exceed four cells, and lie immediately beneath the columnar epithelium of the mucosa. These cells, like the basal cells elsewhere, are pluripotent. Under normal conditions they give rise to cylindric cells. Chronic inflammation and cholelithiasis cause only slight proliferation of the basal cells and only rarely lead to the formation of squamous epithelium from the basal cells. The cancer stimulus, however, causes more active multiplication of the basal cells. They may remain indifferent in morphology, or they may differentiate in two directions, leading to the formation of atypical squamous epithelium or atypical columnar epithelium. Carcinomas of the gallbladder may therefore contain squamous epithelium that has arisen, not by metaplasia of pre-existing columnar epithelium, but by differentiation of indifferent basal cells.

O. T. SCHULTZ.

MALIGNANT TUMOR OF THE CERVIX IN AN INFANT. F. KOHLHAAS, Monatschr. f. Geburtsh. u. Gynäk. **86**:58, 1930.

A malignant tumor of the cervix was noted in a child, aged 16 months, who died of bronchopneumonia. At the age of 6 months, bloody vaginal discharges were the first indications of disease, and thereafter bleeding of several days' duration recurred at intervals of three or four weeks. At autopsy, metastases were found in the para-aortic lymph glands, the liver, the right lung and the right bronchial lymph nodes. The primary tumor had perforated the right common iliac vein, which was thrombosed. The pelvic tumor growth had also compressed the bladder and ureters, so that a large bilateral hydronephrosis resulted. The tumor cells resembled epithelium, and had large, lightly stained nuclei and a large amount of cytoplasm. Some cells were spindle-shaped and resembled fibroblasts. The picture was not that of a pure carcinoma, and much less that of a sarcoma, so that a diagnosis of an immature malignant tumor was made.

GEORGE RUKSTINAT.

A PECULIAR CAROTID TUMOR. B. BAGER, Acta chir. Scandinav. **66**:311, 1930.

A typical carotid adenoma, the size of a hen's egg, was removed from the neck of a man, aged 23, who had a definite enlargement of the thyroid gland. The carotid tumor was situated anterior to the sternomastoid muscle and was not connected with the thyroid gland, but was attached to the carotid sheath by a vascular pedicle. About eighteen months later, a tumor weighing 190 Gm., which was identical with the first, was removed from the left lobe of the thyroid gland. Presumably, the first tumor was an atypically situated carotid new growth the metastasis of which caused the enlargement of the thyroid gland.

GEORGE RUKSTINAT.

Medicolegal Pathology

TRAUMA AND SARCOMA. G. VILLATA, Minerva med. **1**:989, 1930.

A boy, aged 11 years, fell on his hip, and an extensive hematoma developed. Twenty-five days later a growth the size of an orange developed which had a sarcomatous structure. In the center of the tumor was a splinter of bone with periosteum.

POSTMORTEM PHYSICOCHEMICAL CHANGES OF LIVER CELLS. W. LAVES, Deutsche Ztschr. f. d. ges. gerichtl. Med. **16**:61, 1930.

Experimental investigations regarding the physicochemical processes governing the staining of tissues, particularly in relation to the method of Pischinger, are recorded. The author proved that the staining of histologic elements depends not only on the hydrogen ion concentration of the fluids used, but on the electrostatic properties of certain tissue colloids. After death, the hepatic cells, for instance, of the central parts of the acini present tinctorial changes earlier than those on the periphery of the acinus. This interesting study should be read in the original.

E. L. MILOSLAVICH.

CARBON MONOXIDE POISONINGS IN KITCHENS. H. HUG, Deutsche Ztschr. f. d. ges. gerichtl. Med. **16**:72, 1930.

The author presents an analysis of six fatal cases of carbon monoxide poisoning, involving women who used a gas range for boiling laundry in a large wash boiler. A detailed technical discussion regarding the development of carbon monoxide is presented.

E. L. MILOSLAVICH.

SUDDEN DEATH WHILE SWIMMING OR DIVING. MARGULIES, Deutsche Ztschr. f. d. ges. gerichtl. Med. **16**:112, 1930.

According to the author's observations on man and on animals, the drowning process lasts from four to five minutes. A rapid or sudden death is often attributed to a heart stroke or to shock. Distention of the lungs is often found, but it may also be absent. Absence of any signs of hyperaeration of the lungs does not prove that the victim did not drown. Hyperaeration indicates that the person was alive when submerged. Sudden death while the patient is submerged may be the result of the mechanical action or of direct or indirect pressure of the fluid medium or water on the cavities of the body, leading to a mechanical paralysis of the heart. The explanations are based on physiologic and anatomic considerations under various abnormal conditions.

E. L. MILOSLAVICH.

DETERMINATION OF BLOOD GROUP ON CONVICTS. W. HENNEMANN, Deutsche Ztschr. f. d. ges. gerichtl. Med. **16**:126, 1930.

Examination of 310 convicts has shown that there is no definite relation between the blood group and the type of delinquent. The blood groups were proportionately distributed among the dangerous criminals and the habitual and professional delinquents. Group B was not prevalent among persons who committed heinous crimes, as is asserted by other investigators.

MOVEMENTS AND OTHER ACTIONS BY PERSONS FATALLY INJURED. KARL MEIXNER, Deutsche Ztschr. f. d. ges. gerichtl. Med. **16**:139, 1930.

Fractures of the bones of the lower extremities do not exclude the ability to walk. Fractures of the ribs and spine may remain unnoticed by the person injured. Concussion of the brain alone does not cause death, but produces instantaneous unconsciousness. Fat embolism of the kidneys and pancreas should be considered in cases in which death occurred slowly under a coma-like picture. In

certain rare instances, penetrating gunshot wounds of the brain will not cause an immediate collapse, and the critically injured person is able to walk and react. Injuries to the frontal lobes manifest symptoms later than those to any other cerebral area. In young persons, injuries to the head cause concussion of the brain rather than fracture of the cranial bones, which occurs more frequently in older persons. Therefore, in the latter instance, some acts by the injured person are not uncommon, while concussion with the concomitant unconsciousness eliminates any movement. Absence of swallowed blood in the stomach in instances of traumatic hemorrhages from the nasopharyngeal region, but with presence of blood in the lung (aspiration but no ingestion), proves that the unconsciousness occurred simultaneously with the injury; however, one has to consider that severe traumatisms to the skull and brain occasionally occur without rapidly developing unconsciousness. The author discusses gunshot injuries and stab wounds of the heart and the possibilities of their healing. In only a comparatively low percentage of cases does death occur suddenly after stabbing of the heart. Stab wounds of the ascending aorta seem to lead to a fatal end more rapidly than do those of the cavities of the heart. Experience teaches that gunshot wounds of the heart produce a sudden collapse and thus exclude any activity. This is also true occasionally of gunshot wounds of the lung. In not 1 of 185 cases of injuries to the heart produced by blunt violence was the injured person capable of action.

E. L. MILOSLAVICH.

SUICIDE IN FAVOR OF INSURER. W. ELIASBERG, Deutsche Ztschr. f. d. ges. gerichtl. Med. **16**:166, 1930.

An interesting case is reported of a banker who insured his life for a great sum of money and then committed suicide to favor the bank. Detailed criminopsychiatric analysis is presented as to the underlying motives for this action.

E. L. MILOSLAVICH.

SUICIDE WITH A DEVICE FOR SLAUGHTERING ANIMALS. F. WALLBAUM, Deutsche Ztschr. f. d. ges. gerichtl. Med. **16**:174, 1930.

The author gives a description of the instrument and the manner in which it was used. The unusual feature of the case was that the shooting device was placed on top of the head. Two similar cases have previously been described by Schoenberg. In both of the latter instances, however, the instrument was pressed against the forehead.

E. L. MILOSLAVICH.

NETTLE STING (URTICA URENS) BURNS AS CAUSE OF DEATH. E. A. JAKOWLEWA, Deutsche Ztschr. f. d. ges. gerichtl. Med. **16**:180, 1930.

A poorly nourished, anemic and underdeveloped girl, aged 6 years, died suddenly under peculiar circumstances. The skin showed a rash that was interpreted as measles. Investigation disclosed that the foster mother, who often mistreated the girl, in order to punish her because she stole a piece of sausage, undressed her and whipped her with recently plucked nettle until she collapsed. Microscopic examination of the cutaneous rash detected innumerable nettle-stinging hairs within the reddened areas. It was assumed that death resulted from shock.

E. L. MILOSLAVICH.

POISONOUS ACTION OF ZINC SALT SOLUTIONS. R. ZEYNEK and H. WAELSCH, Deutsche Ztschr. f. d. ges. gerichtl. Med. **16**:184, 1930.

In a case of criminal abortion the uterus was irrigated with 0.5 per cent solution of zinc chloride, death occurring one and a half hours afterward. One expert assumed that death resulted from an acute zinc poisoning. The authors deny any action of zinc and base their opinion on experimental proof; they correctly assumed that the fatal end was caused by septicemia.

E. L. MILOSLAVICH.

RESULTS OF AUTOPSY ON EXHUMED BODIES. FERDINAND KLEMP, Deutsche Ztschr. f. d. ges. gerichtl. Med. **16**:190, 1930.

The postmortem observations on twenty-four disinterred and unembalmed bodies are presented in every detail, and the difficulties in correct interpretation of the changes are critically discussed. In only sixteen instances were the corpses well preserved. In disintegration of a dead body, the autolytic, decomposing and putrefactive processes must be considered separately. Autolysis embraces all of the chemical processes that ensue from liberated endocellular enzymes, leading to an autodigestion of the tissues, without any influence of micro-organisms. The decomposition is characterized by processes of oxidation and nitrification liberating heat, the high chemical compounds being transformed into simpler compositions. The putrefaction is the result of bacterial action with subsequent disintegration of tissues to simple chemical substances. The sooner after death chilling of the body occurs, the more retarded is the disintegration. Well nourished, fat bodies, a fluid condition of the blood, external wounds, septic processes, agonal invasion of bacteria, etc., are factors favoring a rapid development of disintegration. Cadaveric rigidity does not necessarily disappear with advanced putrefaction. In instances of potassium cyanide poisoning, a chemical examination is usually futile, since this poison disintegrates rapidly after death. According to the observations, the intestines resist putrefaction longer than the liver, spleen or kidneys. The nongravid uterus remains comparatively well preserved for a long time. The organs of the neck exhibit a remarkably rapid disintegration, while changes are still recognizable in the lungs and the heart. While the membranes of the brain, particularly the dura mater, disappear quite rapidly, the brain itself remains relatively longer.

E. L. MILOSLAVICH.

Technical

THE BOLTZ TEST IN URINALYSIS. A. T. BRICE, JR., Arch. Int. Med. **46**:778, 1930.

Technic: (*a*) Place in a small glass test tube 1 cc. of the filtered or centrifugated specimen to be examined. (*b*) Add 0.3 cc. of acetic anhydride, preferably a brand high in aldehyde content, from a pipet, a drop at a time, with shaking. (*c*) Add 0.8 cc. of concentrated sulphuric acid, from a pipet, a drop at a time, with shaking. (*d*) Let the tube stand at room temperature under observation for five minutes.

The positive reaction is indicated by the appearance of a light lilac to deep purple color. Occasionally, in weak positive reactions the positive color may appear within the five minute period and subsequently be obliterated by the darker colors due to the reaction of other substances in the urine. Occasionally, in strongly positive reactions the positive color may not appear before the expiration of some minutes, owing to the darker colors produced immediately by the reaction of other substances in the urine. In strongly positive specimens the purple color may be so dark as to require dilution of the preparation with water in order to differentiate the purple from possible dark browns or blacks. The prescribed five minutes of the test is a valid test period, as positive specimens have been shown to hold the positive color for several hours. The test with urine is practically impossible to read by any of the artificial lights with which I have experimented up to the time of writing.

The positive reaction is thought to be due to an amino-acid, presumably tryptophan, eliminated in the urine. The test may prove to be more valuable than the test for albumin to demonstrate early or latent conditions of the kidney. There is also evidence that the positive Boltz reaction in urine is of significance in nervous and mental cases and in shock.

ERYTHROCYTE SEDIMENTATION TEST IN TUBERCULOSIS. ANDREW L. BANYAI and SYLVIA V. ANDERSON, Arch. Int. Med. **46**:787, 1930.

A study of the sedimentation test, a modification of the Westergreen method being used, is reported in 2,000 patients. It is shown conclusively that the rate of sedimentation cannot be used for the diagnosis of tuberculosis. The main factor influencing the sedimentation rate is the toxicity of the infection and not so much the extent of the lesion. The greatest merit of the test lies in its value as an indicator of the course of the disease; an increase in the rate indicates an advance in the disease or the onset of some complication, while a retardation in the rate points to improvement.

J. N. PATTERSON.

A NEW DEMONSTRATION OF HORTEGA CELLS. ROBERT R. DIETERLE and META NEUMANN, Arch. Neurol. & Psychiat. **24**:1154, 1930.

The authors use to great advantage Kubie's formulas for silver staining which they recommend instead of the methods of Bielschowsky, del Rio-Hortega, Achucairo and Perdrau. The method for demonstrating Hortega cells, as described, is as follows:

Pieces of brain tissue, from 2 to 3 mm. thick, are fixed in ammonium nitrate, 10 Gm.; formaldehyde (Merck's Blue Label), 70 cc., and distilled water, 430 cc. Frozen sections, 20 microns thick, may be made after from twenty-four hours to three or eight days of fixation. A dozen sections are left for ten minutes in 50 cc. of distilled water plus 5 drops of ammonium hydroxide. The sections are rinsed singly in 100 cc. of distilled water and transferred to Kubie's ammoniacal silver carbonate solution, which consists of the following elements: (8.09 cc. of 28 per cent ammonium hydroxide diluted to 100 cc.; 3.2 Gm. of sodium carbonate dissolved in distilled water up to a final volume of 100 cc.; 10.2 Gm. of silver nitrate dissolved in distilled water up to a volume of 100 cc.; 10 cc. of the latter is put in a 100 cc. volumetric flask, and the diluted ammonia solution is added; it should be shaken vigorously between additions toward the end-point; then 10 cc. of the sodium carbonate solution is added to make up a final volume of 100 cc.; in 50 cc. of this solution a dozen sections are placed at room temperature in the dark). Reduction is done by: formaldehyde (Merck), 10 cc.; pyridine, 10 cc.; mastic, 10 cc. (10 per cent absolute alcoholic), distilled water sufficient to make 100 cc. To 50 cc. of this developer 1 cc. of 1 per cent of hydroquinone solution is added. Development occurs almost immediately. The mastic is dissolved in 96 per cent alcohol; the section is blotted on the slide, cleared in 10 per cent phenol-xylene and mounted in balsam. This method brings out the entire structure of Hortega cells; it shows more of their protoplasmic structure than "any method yet devised." For further minor details the article itself, as well as Kubie's contributions (*Arch. Neurol. & Psychiat.* **19**:888, 1928; **22**:135, 1929), should be consulted.

GEORGE B. HASSIN.

Society Transactions

CHICAGO PATHOLOGICAL SOCIETY

Regular Monthly Meeting, March 9, 1931

JOSEPH A. CAPPS, *President, in the Chair*

PRIMARY, ISOLATED LYMPHOGRANULOMATOSIS OF THE STOMACH. HARRY A. SINGER.

Pathologists have known for many years that lymphogranulomatosis may originate not only in lymph glands, but in any viscus containing lymphoid tissue. The occurrence of primary lesions in the spleen, liver, bone marrow and lungs has attracted little surgical attention because the diagnosis and surgical extirpation of localized lesions is difficult. Primary lesions of the gastro-intestinal tract and particularly those of the stomach manifest themselves promptly, diagnosis is not difficult, and surgical removal is relatively safe.

In the literature seven cases of primary, isolated Hodgkin's disease of the stomach are reported. The preoperative diagnosis was either carcinoma or ulcer, and in all, gastric resection was performed. Five patients recovered and remained well, one died after two years, and the seventh died of obstruction at the stoma a month after operation. No other lesions of lymphogranulomatosis were found post mortem, but microscopic examinations of the various organs are not mentioned. The eighth report of isolated Hodgkin's disease of the stomach, the second in this country, is unique in that a careful gross and microscopic post-mortem examination of the tissues failed to disclose lesions elsewhere in the body.

The clinical diagnosis of isolated lymphogranulomatosis of the stomach is hardly possible in the present state of knowledge. The systemic manifestations are generally absent when the lesion is still in the operable stage. The presence of a soft, flat, infiltrating tumor limited strictly to the distal portion of the stomach, associated with a number of large, succulent, isolated, adenoid-like glands, should suggest the possibility of lymphogranulomatosis. The final diagnosis is made by histologic examination. Inoperable tumors of the stomach should be examined microscopically.

Even in cases in which careful exploration fails to demonstrate granulomatous tissue other than that removed, the prognosis should be guarded. Gross lesions in inaccessible regions and minute foci in the structures examined during operation may escape detection. In cases in which the extent of involvement precludes resection, the patient should be given roentgen therapy.

The complete report will be published in the *Archives of Surgery*.

DISCUSSION

R. H. JAFFÉ: The term lymphogranulomatosis may not be suitable for these lesions. Perhaps malignant granuloma would be better.

E. F. HIRSCH: The implication that all of these lesions are of the character of Hodgkin's disease may be extreme, because there occur in the intestinal tract lesions of granulation tissue which in some respects resemble those of Hodgkin's disease, and yet etiologically are different, as, for example, the chronic changes in the wall of the bowel which occur following traumatic evulsion of the mesentery.

REACTION OF THE BONE MARROW IN EXPERIMENTALLY INDUCED THROMBOCYTOSIS. FRANCIS D. GUNN.

This paper will be published in full in a future issue of the ARCHIVES.

THE EOSINOPHIL RESPONSE IN PERSONS GIVING POSITIVE SKIN REACTIONS TO INJECTIONS OF DICK TOXIN. STUART L. VAUGHAN.

In a general study of the reactions of bone marrow a method for gaining new information on the pathogenesis of scarlet fever has presented itself. In this

disease an early and persistent eosinophilia of the blood has long been recognized as constant. This is also one of the prominent characteristics of allergy, and has led a number of investigators to conclude that allergy has an important rôle in the manifestations of scarlet fever. Recent developments have stimulated interest in the subject.

The experiment consisted of making differential blood counts before and at intervals following the injection of immunizing doses of Dick toxin into a group of eleven student nurses with positive skin reactions, and analyzing the response of the eosinophil leukocytes. The reactions of the skin varied from weakly to strongly positive. The average initial content of eosinophil leukocytes was 0.9 per cent. In every case a decided rise was observed during the course of the injections. The smallest increase was 150 per cent and the greatest was 950 per cent above the normal average. The average increase was 260 per cent. The time of appearance of the eosinophilia varied. In 54 per cent, a marked increase was present within four hours. In two nurses, it was not noted until after the third injection. In the two others with very strong reactions to the Dick test, the eosinophilia was coincident with the appearance of a rash.

These results raise a number of interesting considerations. An increase in the circulating eosinophil leukocytes immediately following the injection of this streptococcus culture-filtrate is contrary to results with filtrates of other bacterial cultures. If eosinophilia of the blood is an allergic response, these results support the contention that a high percentage of persons with positive Dick reactions are sensitized to some constituent of the injected material. That the injections themselves may produce an allergic state or augment one already existing is supported by the delayed increase in eosinophil leukocytes in two cases and a late appearance of maximum increase in others. Evidence is present that the positive Dick reaction may not be allergic. In the two nurses giving the strongest skin reactions, the eosinophilia was not immediate, although susceptibility to the filtrate was shown by the prompt appearance of an erythema. In two other nurses the reaction of the blood appeared only after three injections. The rash, which has been mentioned as the cause of the eosinophilia, was present in but two cases. It may have no causal relationship. Possibly both reactions were the result of the same stimulus. If so, eosinophilia is more easily elicited than a reaction of the skin.

PHILADELPHIA PATHOLOGICAL SOCIETY

Regular Meeting, March 12, 1931

BALDUIN LUCKÉ, *President, in the Chair*

Dr. Warren H. Lewis, of the Carnegie Institution of Washington and Johns Hopkins University, presented moving pictures of tissue cultures of human and mammalian tumor cells, endothelium, capillaries, blood cells and macrophages.

The Annual Conversational Lecture, April 17, 1931

BALDUIN LUCKÉ, *President, in the Chair*

CELLULAR REACTIONS TO FRACTIONS ISOLATED FROM TUBERCLE BACILLI. FLORENCE R. SABIN, M.D.

In following the blood of rabbits infected with large intravenous doses of bovine tubercle bacilli, it has been found that an increase in lesions in the tissues has been reflected by a rise in monocytes in the peripheral blood. These monocytes are often stimulated even to the epithelioid type. On the other hand,

increased resistance on the part of the animal has been correlated with a rise in lymphocytes. These two factors may be expressed in a monocyte/lymphocyte ratio.

Fractions isolated from the acid-fast strains of organisms have given valuable material for testing these theses and for studying the relationships of monocytes to clasmatocytes or macrophages. Tubercle bacilli have been grown under standard conditions by the H. K. Mulford Company, and the lipoidal extracts have been analyzed by Dr. R. J. Anderson of Yale University. The alcohol-soluble lipoid, or phosphatide, produces typical tubercular tissue composed of epithelioid cells and epithelioid giant cells. This action is due to the presence of a new liquid saturated fatty acid, which Dr. Anderson has named phthioic acid.

The immediate reaction to the phosphatide is shown by the relatively immature cells of the milk spots. These cells phagocytose the phosphatide and seem to break it into finer and finer particles, until a typical epithelioid type of cell is reached. This reaction is slow, and the epithelioid cell persists a long time. This type of intracellular reaction is in contrast to clasmatocytic activity. The injection of the tuberculopolysaccharide intraperitoneally is always followed by an emigration of leukocytes that seem to be damaged, for they are phagocytosed by the macrophages and completely disintegrated in about forty-eight hours. Thus, however closely monocytes and clasmatocytes are related, there are two types of cellular activity toward phagocytosed material that may be termed monocytic and clasmatocytic.

The chloroform-soluble material also contains some of the specific phthioic acid, together with an unsaponifiable material, which is intensely acid-fast. This material produces as great a cellular reaction as the phosphatide, but of undifferentiated connective tissue cells. The smooth avian organism dissociated by Dr. S. A. Petroff has relatively little of the wax, for it is but slightly acid-fast and produces a type of tuberculosis that may be called the pure phosphatide disease.

Experiments to test validity of the theory of the relationships of the two strains of cells, monocytes and lymphocytes, to resistance in tuberculosis are under way. An increase in epithelioid tissue induced by the phosphatide has been followed by lowered resistance to bovine infection in rabbits. Experiments testing the effects of increasing lymphocytes are being made at the present time.

Book Reviews

A Text-Book of Medical Jurisprudence and Toxicology. By John Glaister, M.D. (Glas.), D.P.H. (Camb.), F.R.S.E., Professor of Forensic Medicine in the University of Glasgow, etc. In Collaboration with John Glaister, Jr., M.B., Ch.B. (Glas.), M.D. (Hons.) (Glas.), D.Sc. (Glas.), Barrister-at-Law, Inner Temple, London; Professor of Forensic Medicine in the University of Egypt, Cairo, etc. Fifth edition. Price, $8.50. Pp. 954, with 132 illustrations and seven plates. New York: William Wood & Company, 1931.

This book is divided into two sections: medical jurisprudence and toxicology. Under medical jurisprudence are chapters on definitions and scope, medical evidence, personal identity of living and dead in its medicolegal bearings, death in its medicolegal relations (several chapters occupying more than 200 pages), blood stains, medicolegal relations of sexual functions, infanticide, rape, states of insensibility and lunacy in its medicolegal aspects. These matters are presented thoroughly in the light of the laws and customs of Scotland and England and on the basis of a rich personal experience. Many interesting and illustrative cases are cited, with much detail. In the consideration of sudden death, the rôle of embolism is not stressed sufficiently. The various forms of meningeal hemorrhage do not receive adequate attention. The use and value of blood grouping in the identification of persons and of the source of blood stains as well as in the settlement of questions of parentage are not even mentioned. The illustrations in this sections are mostly of gross appearances; the quality of the illustrations is only fair; figures 109 and 117 are worthless.

The section on toxicology occupies 250 pages. It covers the ground thoroughly. The poisons, as well as the circumstances under which various poisonings may take place and their symptoms and the resulting anatomic changes, are described.

This is the fifth edition of the book, "carefully prepared and brought up to date." Of the new matter in this edition, may be mentioned workmen's compensation acts respecting industrial diseases, national insurance acts, dangerous drugs acts, therapeutic substances act and a separate legal index. The senior author has been a teacher of forensic medicine for forty-eight years, and during most of that period he has been engaged in "medico-legal practice for the Crown." The book reflects well the status of forensic medicine and its workings in England and Scotland. It carries with it a certain old-fashioned air of finality, and it is a vast storehouse of medicolegal information, the fruit of years of careful practical work. It will be of interest to those who are concerned with the proper application of medical knowledge in the administration of justice.

Technik der mikroskopischen Untersuchung des Nervensystems. By Prof. Dr. W. Spielmeyer. Fourth edition. Price, 11.80 marks. Pp. 168. Berlin: Julius Springer, 1930.

The progress in any science can be measured more or less accurately by the advancement of its technic, and the fourth edition of Spielmeyer's laboratory guide, which is probably the most extensively used handbook of neuropathologic methods, indicates the comprehensive manner in which the nervous system is now examined. Most of the additions to the previous edition, while not new in the science of neuropathology, are new in the German understanding of that science, for chief among these additions are technical methods from the Spanish school which have been brought into prominence outside of Spain by the American workers Penfield and Globus. In fact, the book is more international than its previous editions.

The order in which the material is presented, as in the previous editions, goes more or less hand in hand with the manner in which the nervous system is prepared and examined. An introduction explaining the principles of fixation, embedding and cutting and the preparation of certain general chemicals, such as hematoxylin, precedes the more specific parts. The fine hematoxylin of Ehrlich seems to be omitted from, and Meyer's hemalum added to, the old list.

In the methods of staining the nerve cells, several of the less desirable methods have been omitted, as has the polychrome methylene blue for the medullary sheath. Marchi's chromosmium method has been removed from its place among the stains for the medullary sheath and has been placed with methods for studying the products of disintegration.

The chief changes are in the technic of staining glia, as mentioned; Anderson's method and several modifications of Hortega's method by Penfield, Globus and Kanzler have been added, while several of the less specific methods have been omitted.

In the study of the products of disintegration, of deposits and of the histochemical aspects, one finds a new fat stain, sudan-orange; von Braunmühl's silver method for senile plaques, and a new oxydase reaction, while several methods of staining frozen sections in order to detect spirochetes and a method of staining to detect Negri bodies improve the chapters on micro-organisms.

HANDBOOK OF PROTOZOOLOGY. By RICHARD ROKSABRO KUDO, D.Sc., Assistant Professor of Zoology, University of Illinois. Price, $5.50. Pp. 451, with 175 etchings containing 1,463 figures. Springfield, Ill.: Charles C. Thomas, 1931.

In presenting this "Handbook of Protozoology" the author has probably supplied a long-standing need. As suggested in the preface, the study of the protozoa as a group is becoming more and more widespread in universities and colleges. The need for an introductory volume dealing with the biology of the protozoa in general and giving adequate figures of representatives of the various groups has apparently been supplied.

The introductory chapter deals with general points of morphology, as well as the relationship of protozoology to the biologic sciences as a whole. This chapter also contains a good review of the history of protozoology. The next two chapters contain discussions of the morphology and physiology of the protozoa, considering structure, reproduction, etc. The following thirty odd sections, almost the entire book, are devoted to classification and brief discussions of the various genera, species, families, etc., throughout the entire protozoan group. Representative members of the groups are pictured, and these figures have been generously supplied. It is in these chapters that the real worth of the book lies. There are many monographs on the various taxonomic groups, but this contribution is unique in that it gives in concise fashion a consideration of each division of the entire group, from the flagellates through *Sarcodina* and *Sporozoa* to the ciliates. The free and parasitic forms are given equal stress. The book is appended by a rather brief consideration of the collection, cultivation and observation of protozoa.

The illustrations deserve further comment. It is stated by the author that they have all been redrawn especially for the work. They are dependable representations of the forms, and credit is due for the quality of their execution, which greatly enhances the value of the book. The make-up, as well as the clarity with which the figures have been reproduced, contributes to the formation of a volume with a pleasing appearance.

Books Received

A Textbook of Laboratory Diagnosis with Clinical Applications for Practitioners and Students. By Edwin E. Osgood, M.A., M.D., Assistant Professor of Medicine and Biochemistry, Director of Laboratories, University of Oregon, School of Medicine, Portland, Ore., and Howard D. Haskins, M.D., Professor of Biochemistry, University of Oregon, School of Medicine. Price, $5. Pp. 475, with 26 illustrations. Philadelphia: P. Blakiston's Son & Company, 1931.

The Division of Laboratories and Research of the New York State Department of Health: A Short Account of Its History and Present Status. By A. B. Wadsworth, M.D., Director. Albany: 1931.

The Physician of the Dance of Death: A Historical Study of the Evolution of the Dance of Death Myths in Art. By Aldred Scott Warthin, Ph.D., M.D., LL.D., Professor of Pathology and Director of the Pathological Laboratories in the University of Michigan, Ann Arbor, Mich. Price, $7.50. Pp. 142, with 92 illustrations. New York: Paul B. Hoeber, Inc., 1931.

Food Poisoning and Food-Borne Infection. By Edwin Oakes Jordan, Chairman of the Department of Hygiene and Bacteriology, The University of Chicago. Price, $2.50. Pp. 286. Chicago: The University of Chicago Press, 1931.

Noguchi. By Gustav Eckstein. Pp. 418, with illustrations. Price, $5. New York: Harper & Sons, 1931.

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